BEDSIDE URINE-TESTING.

G. OLIVER, M.D.

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ON

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A CLINICAL GUIDE TO THE OBSERVATION OF URINE IN THE COURSE OF WORK

BY

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PREFACE.

THE second edition of this little work, which passed out of print twelve months ago, has formed but the nucleus of this its successor.

The additions comprise chapters on several departments of urinary observation not handled in the previous editions, and the results generally of the labours of the past winter in this important branch of clinical enquiry.

The aim of these pages is to supply in the compass of a pocket companion the leading data in regard to urinary

observation; to point out what ought to be noticed in the course of work; and to indicate the readiest methods of testing by which the practical aspects of morbid urine may be brought home to the senses with the least expenditure of time and trouble: in a word, to facilitate that oft-neglected part of practice—the examination of urine in all cases,—which every now and then either provides a new insight, or sheds a corrective light.

I have endeavoured throughout to keep steadily in view the practical character of my design: hence the exclusion of theoretical questions from the text, and the mere occasional reference to such matters—when apparently suggestive—in the foot notes.

The original matter, which has been drawn forth by the infallible method of the cross-questioning of nature by repeated and varied experiment, cannot be justly gauged by those who have not followed the track which led to it. However, any quickening truth which it embodies must live, divested of everything that cannot, and should not, survive the crucible of observation and experience —the Baconian test of all progress.

Harrogate,
June, 1885.

"Those, therefore, who determine not to conjecture and guess, but to find out and know; not to invent fables and romances of worlds, but to look into, and dissect the nature of this real world, must consult only things themselves. Nor can any force of genius, thought, or argument be substituted for this labour, search, and inspection."

—*Instauratio magna.*

"Practice is laborious either from the multitude of instruments, or the bulk of matter and substances requisite for any given work. Those instances, therefore, are valuable, which either direct practice to that which is of most consequence to mankind, or lessen the number of instruments or of matter to be worked upon."

—*Novum organum.*

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INTRODUCTORY.

The Aim of Bedside Urinary Testing is to ascertain, in the ordinary course of medical observation, the condition of the urine: either to detect leading pathological states of this excretion, as immediate aids to diagnosis and treatment; or—as in the majority of cases—to definitely eliminate them from the clinical view.

Whether the evidence, thus revealed without delay, be positive or negative, it may be equally valuable to the practitioner at the moment, either by giving a turn to his investigation, or by correcting impressions suggested by other data: but, besides thus serving this immediate end, it enables the busy man to readily weed out on the spot the important urines for particular investigation at home, and reduces the liability

to omission of that important part of clinical observation—urinary examination in all cases.

The testing of urine should, therefore, be rendered as ready and portable at the bedside as are other instruments of clinical enquiry—such as the thermometer, the stethescope, &c. To this end the following pages are devoted.

The Tests I propose are in the form of test-papers[1]: than which I cannot conceive of anything more convenient for bedside work. They are specially fitted for this service by virtue of their possessing all the essential qualities which should pertain to such tests; namely, trustworthiness, stability, portability, and freedom from causticity and other objectionable properties. The reader has merely to call to mind the miseries of nitric acid and of Fehling's solution—the urinary cases dilapidated, and articles of clothing spoilt by these destructive reagents—in order to realize how unsuitable are such caustic tests for pocket use; and

[1] The strips of chemically charged paper are but vehicles for the ready application of the reagents.

he must then regard with some sense of relief the neat and cleanly methods provided by the test-papers, which can be as freely handled, and as harmlessly—to the fingers and to the tests—as ordinary writing paper.

Then again, no other dry preparations —such as pellets, powders, &c.—can compare with test-papers in readiness for use, and in providing in so small a compass a series of tests for determining several points of clinical importance in the examination of urine.

Moreover, the test-papers, apart from ministering to the personal convenience of the observer, possess clinical advantages, such as the handy and time-saving methods which they provide for quantitative estimations.

CHAPTER I.

THE GENERAL CHARACTERS OF THE URINE.

I. On Selecting a Specimen of Urine for Examination.

Wherever practicable, the urine of the whole twenty-four hours should be reserved. If this, however, cannot be done, the observer should direct the portion passed two or three hours after breakfast, and that voided on rising, to be kept in separate vessels. These specimens will provide a fairly good average when mixed in equal porportions; and when examined separately will afford information as to the effects of digestion, and of fasting and rest. On no account should the observer rely on an examination merely of the urine passed in the morning before breakfast; for it may be free from albumin or sugar, or nearly so, while the speci-

mens voided during the day (after meals) may contain these constituents in fair proportions, or in larger quantities. (See pages 144 and 195).

The Urine has deposited.— Urine reserved for examination has usually stood for some hours, and has consequently allowed any matters in suspension, that can subside, to settle. The observer will often require to examine separately the supernatant portion and the deposit; and should, therefore, see that the vessel containing them is not shaken. Besides, this precaution has special reference to testing for albumin and bile-acids, when it is highly desirable, if not essential for accurate observation, to select a transparent portion of the urine.

The nipple-pipette (see chap. xiv.) is a most useful article at the bed-side; for it enables the observer to take up a perfectly clear specimen of urine—perhaps otherwise unprocurable—and to examine separately the deposit, or any particular portion of it.

The specimen is turbid.—If a transparent specimen is not provided, and if the turbidity does not clear up on adding a citric acid test-paper, or with warmth, the observer had best filter it; and, for this purpose, his urinary case should be furnished with a few pieces of filtering paper—one of which, rolled into a cone, and held over the test tube, will, in a minute or two, provide a sufficiency of transparent urine for albumin, bile-acid testing, &c.

II. The Odour.

Healthy urine emits a characteristic aromatic odour, varying, however, with different individuals, and with the degrees of concentration of the urine. A strong urinous odour is often emitted when the percentage of urea—and in fact of the total solids—is high. The urine of dyspepsia sometimes emits a sickly odour.

Alkaline Urine.—The urine, without being ammoniacal, often smells of the bladder, when feebly acid or alkaline, and when slight catarrh of the urinary

passages exists. When alkaline from fixed alkali, it exhales an odour like that of horse's urine. When the urine contains ammonium carbonate, derived from the decomposition of urea, the odour becomes 'ammoniacal': and this may be the case when it is voided, or shortly afterwards, or after standing some time in a warm room.

Urine emits a 'putrescent' odour, when it contains much decomposing organic matter, as in destructive disease of the bladder, kidneys, &c.

Sugar.—The presence of sugar is often attended by a sweet smell, as that of new hay, or whey; and in diabetic coma, the urine emits an odour like that of chloroform. Saccharine urine in a state of fermentation smells like 'turned' milk.

Cystin.—Urine containing cystin at first smells like sweet-briar, but speedily becomes horribly offensive — emitting sulphuretted hydrogen.

Medicines, &c. — Certain medicines (turpentine, copaiba, cubebs, oil of sandlewood) and articles of diet (aspara-

gus, garlic) communicate their characteristic odours to the urine.

III. The Consistence.

Healthy urine is always watery; but in disease, the consistence may be so increased, from the presence of mucus or muco-pus, as to prevent the urine from running into drops—for when poured from vessel to vessel it flows out *en masse*.

Alkaline Purulent Urine.—If the urine be purulent and alkaline there will be seen a glutinous mass—consisting of pus transformed by ammonium carbonate into a mucous looking substance—which adheres tenaciously to the bottom of the vessel.

Chylous Urine.—In chyluria the consistence of the urine is increased. (See pp. 33, 34).

Albuminous Urine.—When albumin is present in considerable quantity, though the consistence is not obviously, or is only slightly increased, the splash of the urine is softer and less watery; and, after shaking, the froth remains intact

much longer than that of non-albuminous urine of the same specific gravity.[1]

IV. The Colour.

The tint of normal urine ranges from straw yellow (*urina potus*) to golden amber (*urina sanguinis* and *urina cibi*); the depth of colour varying with the concentration—abundant and watery urines being pale, and diminished discharges of higher specific gravity being darker. This rule is of pretty general application.

Pale Urines.—When the urine is pale, the observer will bear in mind conditions that induce a copious flow; such as cold weather, the free taking of fluids, hysteria and other neurotic ailments inducing paroxysmal attacks, anæmia and chlorosis, diabetes (mellitus and insipidus), and chronic Bright's disease—especially the waxy and granular kidney. The urine of women is paler than that of men; and also the urine of persons of feeble general health—as during convalescence from acute

[1] The reader will bear in mind that other than albuminous urines may provide a 'stable froth,' such, for example, as those well charged with solids—the sp. gr. being over 1020.

diseases, &c.—than of the robust. Pale urines suggest the absence of fever.

Dark Urines.—On the other hand, dark urines are often also concentrated, as during warm weather, after active exercise, in diarrhœa, in fevers, and in disorders of the liver. Dark urines suggest increased tissue-change.

(a) **Indican.**—High coloured and concentrated urines frequently contain a large quantity of indican[1]—a substance which yields free indigo when broken up by the per-acid state of the secretion; hence the blue, or violet, or reddish violet, or green tint, which appears in such urines on standing, and best seen at the surface near the sides of the glass vessel containing them.

An increase of indican, and the occasional appearance of free indigo in the urine, have been observed in many pathological conditions: but they are, for the most part, such as disturb or delay intestinal digestion; *e.g.*, obstructive diseases of the bowels, dysentery, diarrhœa, typhoid

[1] An excess of indican is also sometimes found in pale urines.

fever, cirrhosis of the liver, cancer of the liver, cancer of the stomach, peritonitis, the reaction of cholera, lymphoma and lympho-sarcoma of the abdomen, Addison's disease, and diseases and derangements of the entire central and peripheral nervous system.[1] Jaffé has shown that indican is greatly increased in obstruction of the small intestines and general peritonitis, but only slightly so in obstruction of the large intestine. Senator has observed an increase in granular kidney, but not in other forms of chronic renal disease.

(b) **Melanin.**—A black pigment (melanin) is present in the urine of patients suffering from melanotic tumours—especially of the liver and the skin—and sometimes also in ague. In these cases the urine may be of normal colour when passed, but becomes black on standing, or on the addition of an acid.

(c) **Blood.**—When the urine presents a smoky hue, the observer will suspect the

[1] This statement summarizes the clinical observations of Jaffé, Neftel, Wyss, and Robin.

presence of a small quantity of blood; but when in larger proportion, blood communicates a distinctive red colour (see p. 31). When the colouring matter of the blood corpuscles is present (hæmoglobinuria or hæmatinuria) in large quantity, the urine is as dark in colour as port wine (see p. 32).

(d) **Bile.**—Bile is also a cause of dark urine. (See p. 199).

(e) **Medicines, &c.**—The urine may be dark, or even black, when carbolic acid or creosote has been taken in large quantity.[1] Certain vegetable substances, in passing out by the urine, communicate their distinctive colours; such as rhubarb, logwood, whortleberries, indigo, madder, &c. Santonin gives a yellow bile-like colour to acid urine, which moreover, further resembles biliary urine in staining the linen of the patient, but is easily distinguished by striking a crimson reaction on adding

[1] Carbolic urine may be pale when voided, but becomes dark on exposure to the air. Pyrocatechin (a normal constituent of horses' urine) in rare cases appears in human urine, which is likewise of ordinary colour when passed, but darkens on standing, or immediately on adding an alkali. (Ebstein and Müller).

a carbonate of soda test-paper to 60m of the urine. When chrysophanic acid (present in rhubarb and senna leaves) is eliminated by alkaline urine, it provides a red tint like that of blood; but it differs from the latter, by at once paling into yellow, when a citric acid test-paper is dropped into 60m of the urine, and by the red colour reappearing on alkalinizing the acidified urine by a sodæ carb. test-paper.

V. On Cloudiness and on Deposits.

Healthy urine should be perfectly bright and transparent when voided, and should remain so—only in the course of a few hours permitting a light flocculent cloud to fall. The slight loss of clearness of a fresh sample should be carefully noted, by holding it in a test tube up to the light, and shaded by the hand; and the cause of the opacity should be ascertained. The degrees of turbidity of course vary—from the merest trace to the most dense.

Urine may be cloudy when passed, or it may become so as it cools. In the latter

case the cloudiness is almost invariably due to urates falling out of solution—a source of turbidity which does not apply to freshly voided urine, unless the urine is passed into a cold vessel.[1]

The suspended matters, which destroy the transparency of urine, may be inorganic, or organic, or both.

1. *Inorganic causes of turbidity.*

These are for the most part Urates and Phosphates.

(*a*) **Urates** (*amorphous*) form the common cause of the turbidity of urine; and are distinguished from others by quickly vanishing when the urine is merely warmed, even by a comparatively low degree of heat, *e.g.* 100° F.

As a rule the opacity settles pretty quickly and completely; slowly, however, if the specific gravity is above normal,[2] or

[1] An exception to this rule is found in the comparatively rare cases, in which chrystalline urate of soda falls out of solution in the urinary passages—as occasionally happens in gouty subjects, and in children.

[2] Dr. Garrod tells me, that he lately met with a urine of sp. gr. 1054, in which urates fell out of solution, and remained as a permanently diffused opacity.

the urine contains organic constituents. Albuminous, mucous, or bloody urine may remain for some time hazy from this cause. The colour of the turbidity varies from a fawn to a flesh tint (see p. 42).

It is characteristic of urines which deposit lithates, to provide on standing a bluish scum on the surface, best seen at the sides. Urines that let fall red-tinted urates generally contain indican (see p. 22).

The clinical significance of a turbidity due to amorphous urates may be *nil*, as when it arises from concentration of the urine, and an increase of the acidity: as from violent exercise with perspiration, from abstinence from fluids, or from a bilious attack, or from cold weather; when it is only occasional. When frequent or persistent and of a flesh-tint (lateritious), there may be fever (inflammatory or not), organic disease, or some cause of rapid wasting of tissue.

(b) **Phosphates** *(earthy.)*—Every now and then the reader will come across a urine which when voided is milky, but

which clears up completely on dropping into 60m of it a citric acid test-paper. In such cases the cause of the opacity is due to earthy phosphates, which do not dissolve simply because the urine is of an alkaline, neutral, or merely of a feebly acid reaction. No other form of cloudiness is removed by a citric acid test-paper; hence, when it is only in part removed by this means, some other source or sources of turbidity exist, such as pus, blood, bacteria, &c. Phosphatic cloudiness (either consisting entirely of earthy phosphates, or of these along with pus) is distinctly white or milky, and is increased by heat.

2. Organic causes of Turbidity.

The principal organic products that impair the clearness of urine are—

(*a*) Pus and muco-pus.
(*b*) Blood.
(*c*) Oil-globules.
(*d*) Organisms.

The loss of transparency due to these causes is apparent in the freshly voided

urine; and differs from cloudiness referrible to urates and phosphates, by not clearing up either with heat, or with a citric test-paper.

(a) **Pus.**—A very small amount of pus suffices to give a haziness to the urine held up to the light; though it is true the haze induced may be only slight. The presence of pus is pretty certain if the fresh urine contains bacteria (see p. 35) and a small quantity of albumin. The opacity due to pus differs from that caused by blood, in being whitish or greyish.

If purulent urine contain much mucus or albumin, the pus will subside but slowly—the turbidity remaining for hours; while, on the other hand, if mucus or albumin is present only in small quantity, the subsidence will be rapid, the urine being left clear, or perhaps only slightly turbid from bacteria (see p. 35.) Purulent urines always contain albumin—in proportion to the amount of pus—in the absence of any other source of albumin.

Mucus, quite apart from pus, is in itself not a cause of turbidity; but it

becomes so, by forming a nidus, as it were, for the deposition of cellular elements—pus, blood, &c.—and of amorphous urates and phosphates. When present in excess, mucus communicates a glairy or glutinous character to the urine throughout, and does not specially provide a deposit. The faint cloud that forms in the body of the urine shortly after being voided, and then slowly subsides, is mucus along with epithelium derived from the genito-urinary passages. It is larger in women, the vagina providing mucus and cellular elements (epithelium and pus).

The Clinical significance of Pus.—Pus is the common source of the small quantities of albumin so frequently encountered in urine, especially in that of women; the slightest vaginal discharge, even in children, leading to the contamination.

An inflammatory irritation of any portion of the mucous lining of the urinary passages creates a purulent exudation which mixes with the urine, *e.g.*, of the urethra (gonorrhæa and gouty urethritis),

bladder (cystitis from any cause), pelvis of the kidney (pyelitis).

The observer will also bear in mind the bursting of an abscess into the urinary passages, *e.g.*, perineal, peri-vesical, peri-renal.

(*b*) **Blood.**—The presence of blood, even in very small quantity, impairs the transparency of the urine, and generally communicates a *distinctive colour:* a reddish tinge, if the reaction of the urine is alkaline, or the quantity of blood is more than $\frac{1}{5}$ of a *per cent.*; and a dull smoky appearance, if the urine is acid, or the amount of blood is small. When the blood is of renal origin, the urine is usually smoky, and lets fall a dirty brownish deposit; but when otherwise, the urine is more distinctly red, and clots may be detected.

Urine containing blood is always albuminous; and when coagulated the clot is brown-tinted.

If the urine is muddy and dark—even as dark as porter or port wine, but devoid of the clearness of jaundiced urine of that depth of colour—and has let fall an abund-

ant chocolate-looking deposit, and is, moreover, highly albuminous—the albumin coagulating into brownish instead of the ordinary white masses on boiling, and on separating leaving the urine as dark as before—in all probability the observer is dealing with a case of *hæmoglobinuria*—a paroxysmal disease in which the red-corpuscles are dissolved, and the liberated hæmoglobin thus passes out with the urine. There are lesser degrees of this ailment, in which, during the paroxysms, the urine may be merely dusky, providing a smaller deposit—of the same character however—and containing proportionately less albumin.

If the observer wishes to examine a suspicious urine at home for blood by the guaiacum test, he will find a slip of white blotting paper, dipped in the urine and dried, a convenient vehicle : then it will only be necessary to let fall a drop of the tincture of guaiacum on it, followed by a drop or two of ozonic ether or of spirits of turpentine; when the characteristic blue colour will appear if blood is present.

The clinical significance of blood.—Blood may proceed from any part of the urinary apparatus—from the tubuli uriniferi to the urethra. The principal causes of urinary hæmorrhage may be classified thus:

Traumatic. External injury. Renal calculi. Diminutive concretions in tubuli uriniferi.

Morbid Growths, &c. Cancer. Tubercle. Parasites. Fungoid growth (bladder). Varicose veins (bladder).

Renal Congestion, &c. Passive (heart disease). Active (acute nephritis, effects of turpentine, cantharides). Chronic Bright's disease (blood in microscopic proportions as a rule).

Symptomatic. Hæmoglobinuria. Purpura. Scurvy. Malaria. Eruptive fevers, &c.

Vicarious. Menstrual.

(c) **Oil-globules.**—Urine containing particles or globules of fatty matter presents a milky appearance, always contains albumin, and often blood (then the urine has a slight rose tint), peptones, and sugar. Chyluria is the principal clinical example of this kind of urine; the characteristic feature of it is a fibrinous clot, which rises to the surface, forming there a white or pinkish jelly-like layer, and leaving the urine below still

turbid, though less so than when voided; and the consistence of the urine is increased in proportion to the number of fatty molecules. Sometimes in this ailment the fat globules are absent; but there is fibrin (as indicated by the formation of a coagulum like that of calf's foot or currant jelly) and also albumin; in other words the urine is *lymphous* not *chylous*[1].

(d) **Organisms.**—The principal microscopic organisms that give rise to turbidity of fresh or recently voided urine are Bacteria and Spermatazoids.

The common rod-bacterium, or Bacterium Termo, or Vibrio, is frequently encountered in large numbers in urine just voided—as well as, of course, in stale urine.

According to my observation, it is much more frequently met with in the fresh urine of women than in that of men; a difference which appears to be traceable to the prevalence of these active vitriones

1 See *Urinary and Renal Diseases*, by Wm. Roberts, M.D. 1885.

in the vaginal secretions, and the migration of them through the short urethra into the bladder, where they may swarm in the newly secreted urine.

The slight opacity induced by these organisms is characterized by two features:

(1) It does not settle, however long the urine is set aside: the upper portion remaining as fully charged with the bacteria as the lower.

(2) When the urine, contained in a test tube, and shaded by the hand, &c., is held up to the light and agitated, it is seen for the moment to become traversed throughout by fine silky waves, which interlace. Whenever I have observed this peculiar waviness in fresh urine I have invariably found by the microscope either these rod-bacteria or spermatazoids; but in the latter case the opacity settles.

The urine in this form of bacteruria generally contains a trace of albumin from purulent contamination; the reaction of it is either only slightly acid, neutral, or somewhat alkaline; and it is more disposed

than normal urine to undergo ammoniacal fermentation.

The presence of the Bacterium Termo does not, as a rule, set up any marked local symptoms. Sometimes, however, I have noted slight irritability of the bladder, and a diposition to nocturnal micturition. Of course when cystitis existed—and this bacterium is often to be detected in the fresh urine of cystitis—there were the usual symptoms.[1]

3. *Deposits.*

(*a*) **Epithelial.**—Epithelial débris collects in the light flocculent cloud that falls from all urines: it is more abundant in women than in men; and in all cases fine flaky particles are to be observed. In men who have had gonorrhæa, or who are affected by some prostatic irritation, there are seen to float through the freshly voided

[1] Dr. Wm. Roberts has described a form, or rather two forms of bacteruria, differing from that associated with the Bacterium Termo, mainly in three respects: no unusual disposition on the part of the urine to undergo decomposition; complete subsidence of the organisms in the urine; and rather prominent local symptoms—dysuria, and the like. (*On Urinary and Renal Diseases*, 1885, p.p. 176—183.)

urine many small stringy-looking flocculi, which eventually gather in the light mucous-like deposit.

(*b*) **Uric Acid**—The only sediment recognizable by the naked eye as separate grains or crystals of a reddish brown colour is *uric acid*, in the form of 'red sand' or 'cayenne pepper grains,' or fine 'red specs.' This deposit is observed on the sides of the glass as well as at the bottom: and the particles vary greatly in point of size, not only in different urines, but in the same sample—from mere dust to coarse sand; when in a fine state of division, uric acid resembles lateritious urates in appearance, but is readily distinguished by warmth failing to dissolve it. Urines that deposit uric acid are always acid—often per-acid.

The clinical significance of Uric Acid deposits.—The precipitation of uric acid sand is definitely pathological, if it takes place before the urine is voided—the uric acid crystals being discharged with the urine—or as the urine cools. It implies acidity of the urine, and, as a rule, a lower density

than obtains when urates fall: hence, it often happens that urates separate first, and uric acid afterwards. The deposition of urates is determined mainly by concentration and temperature along with an acid reaction: while that of free uric acid is less affected by temperature than by acidity and a reduced density. Uric acid deposits are apt to occur when the action of the skin is checked, as in cold weather, or when there exists extensive disease of the skin (eczema, psoriasis) or when the tegument is harsh and dry; and when the diet is, for the individual requirements, too rich in nitrogenous elements. They often precede glycosuria, or alternate with the appearance of sugar. A shower of uric acid crystals is apt to follow a gouty attack.

All other deposits—so far as the naked eye can recognize—are amorphous. In colour they vary greatly: being either white or greyish, fawn, pink, red, or dark brown.

(*c*) **Light-Coloured Deposits.**—When white or greyish, they are likely to consist

of *earthy phosphates*, or *pus*, or *both:* and this presumption will be confirmed, if the reaction of the urine is alkaline, neutral or only faintly acid; and, furthermore, if there be an iridescent scum on the surface. If, on transferring some of the sediment to the test tube, the opacity completely vanishes on adding a citric test-paper, it is due to *phosphates only:* if it is not thus clarified, it may arise from *pus* or possibly *urates of a light colour:* and if it is only in part cleared up by the acid, it may be ascribed to *phosphates along with pus.* A phosphatic opacity is always increased by heat. It implies either a lowering of the acidity of the urine to the verge of neutrality, or an alkaline reaction: and does not signify an increased elimination of phosphates.

A trace of albumin in the supernatent urine provides presumptive evidence in favour of the deposit containing *pus*: and this is confirmed by the failure of warmth to reduce the turbidity. If the deposit adheres tenaciously to the bottom of the vessel—when the urine will be am-

moniacal—and, from its great viscidity, can be drawn out into ropes, its purulent nature is unquestionable. When, however, the urine is acid, pus is not thus transformed into a tenacious mucous-like mass.

Light coloured *urates* may fall from urines of comparatively low specific gravity.

Oxalate of lime also provides a light coloured deposit. Dr. Wm. Roberts thus aptly describes the naked-eye characters of it as it appears in the urine-glass. "The sides of the glass are seen to be traversed by very numerous fine lines, running in bands, transversely or obliquely, giving an appearance as if the glass were finely scratched. This appearance is due to the crystallization of the oxalate on the fine lines or inequalities left after cleaning the glass by towelling. The subsided portion is equally peculiar, it consists of two parts—a soft pale-grey mucous-looking sediment occupying the bottom of the vessel, and overlying this a snow-white denser layer with an undulating but sharply limited surface. The only other substance which crystallizes in

lines on the sides of the glass is uric acid; this is easily discriminated by the greater coarseness of the lines, and their more or less brown colour."[1] The *clinical significance of oxalate of lime*, when it forms a copious and persistent deposit, is a somewhat disputed matter. There is no doubt that certain vegetables increase it: such as onions, tomatoes, rhubarb, turnips, &c.; but, apart from this dietetic source, there are certain well defined pathogenic conditions that favour the deposit: such as,

(1) Fermentative dyspepsia: fatty acids (butyric, acetic, lactic) being generated that impede the development of the blood discs, and thereby lower the oxygen-carrying power of the blood—oxidation halting at oxalate instead of proceeding to carbonate.

(2) Insufficient supply of oxygen from some impediment to respiration (emphysema, &c.,) or from impurity of the atmosphere, or the food (especially sugar and starch) in

[1] *Op. cit.*, pp. 80, 81.

excess of the oxidizing power. In a word, impeded metamorphism from deficient oxidation.

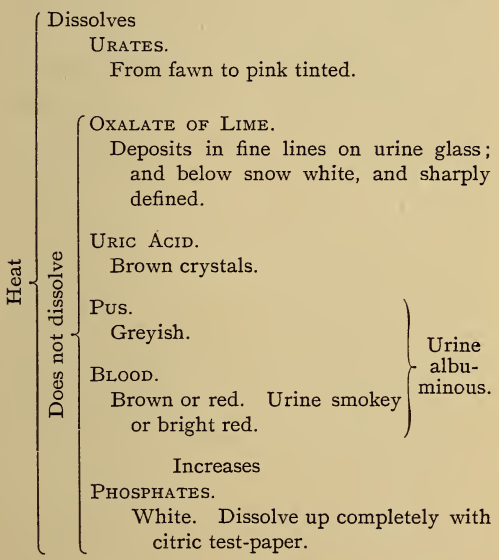
(3) Depressed nerve-tone.

(d) **Dark Deposits.**—Deposits of a darker hue—from fawn to chocolate-brown—are mostly due either to urates, or to a blood product.

Sediments consisting of *urates* vary in colour from light brown to a pronounced flesh tint; and they always fall from urines distinctly acid — generally per-acid. The depth of colour is in a general way proportionate to the specific gravity; being fawn-tinted when the specific gravity is from 1016 to 1018, and pink-tinted when the degrees are higher. Warmth always clears up an opacity due to urates.

Deposits of a dirty brown or chocolate colour, or bright red, and especially when consisting of clots, are probably *blood-derived:* and this suspicion will be confirmed or negatived by detecting albumin in the supernatent urine, or failing to do so; and by the colour of the urine (see p. 31).

The foregoing characters of urinary deposits, as they appear to the naked-eye, may be thus epitomized :—



On collecting a deposit for examination at home by the microscope.—It is frequently advisable to obtain the sediment derived from the urine of 24 hours: as for example, when, in searching for casts in a doubtful case,

a specimen of the urine passed during the day has not provided positive information. In many urines, especially when the amount of albumin of renal origin is small, very few casts are present: or they are absent from one discharge of urine but appear in another. Then the examination of the whole deposit of the day's urine will enable the observer to decide the matter with more certainty, and with greater facility, than that of several ordinary specimens. The whole 24 hours' urine should be allowed to settle, and the clear part poured off from the sediment contained in the last six or eight ounces, which should be reserved for the microscopical examination.

VI. The Daily Quantity of Urine.

The average daily discharge may be roughly estimated at fifty ounces, and the ordinary variations pertaining to the same person, as well as to different individuals, may be gauged at one third above or below the mean amount.

The quantity is excessive.

(a) **The increase is temporary.**—This may arise from cold, nervous excitement, a fit of hysteria, an asthmatic attack, copious drinks, or diuretics.

(b) **The increase is persistent.**—As in diabetes mellitus and insipidus, and in the course of waxy and granular (the cirrhotic) kidney.

The quantity is diminished.

Reduction of the urinary flow occurs when fluids are taken habitually in small quantity; when the skin and lungs are unusually active, as in hot weather—especially when exercise is taken—and in fever; when the kidneys are embarrassed, as in congestion from heart disease, in acute inflammation, in sub-acute inflammation in the course of Bright's disease, in some forms of renal disease throughout, and towards the close in all varieties; when vomiting or diarrhæa is persistent, as in cholera; and when the bowel is obstructed — as in acute strangulation

high up. The urine is also greatly reduced in quantity in most hepatic diseases and disorders, and always in cirrhosis of the liver.

The urine is suppressed.

Failure of the urine to appear in the bladder may arise from either mechanical obstruction (obstructive suppression) or from organic disease or obscure disorder —neurotic or vascular—of the kidneys (non-obstructive suppression).

(*a*) **Obstructive suppression:** as from a calculus impacted in the ureter—there being only one kidney (congenital defect) or only one workable kidney; vesical tumour closing up the ureters, &c.

(*b*) **Non-obstructive suppression:** as in acute nephritis—especially the form that follows scarlatina; and in chronic Bright's disease—at the close; in cholera and yellow fever; in fever and inflammations generally—when intense; in shock—especially from cathetering and other operations on the urethra; and in hysteria.[1]

[1] See Charcot's *Diseases of the Nervous System.* New Syd. Soc.

The nocturnal discharge of urine.

When the kidneys are healthy a much larger proportionate quantity of urine is excreted during the day, than during the night. The practitioner turns this physiological fact to good clinical account, when he suspects chronic renal mischief or diabetes, as soon as he discovers an increase of the quantity of urine discharged in the night. In some forms or stages of atrophic degeneration of the kidneys (cirrhotic especially) the nocturnal rise of urine is very considerable; and whenever it occurs, it calls for enquiry.

CHAPTER II.

THE SPECIFIC GRAVITY OF THE URINE

Pocket Urinometers. — Some time ago I made a good many observations on the working of the small pocket urinometers in general use, in order to test the readings they provide—how far they are reliable. I found these little instruments of precision merely so in name and appearance: for they were liable to a wide range of error—at least from five to seven degrees. I, therefore, regard them for clinical purposes as valueless and misleading.

The Author's Method.[1]—For taking the specific gravity—and especially at the bedside–I greatly prefer a glass bead accurately representing 1008, (ch. xiv). This is dropped into the graduated test-tube (ch. xiv) and the urine is added to the lowest

[1] The idea of obtaining the specific gravity by dilution was suggested to me by Dr. S. C. Smith, of Halifax, in the course of a discussion on my method for quantitative albumin at the Leeds Medico Chirurgical Society.

mark: if the specific gravity is below 1008, the bead at once falls to the bottom of the tube; but if—as in nearly all urines—it is higher than this figure, the bead floats up to the surface—the rapidity of the motion being greater as the specific gravity is higher. If now, the observer adds water, little by little, and with some force, so as to mix well with the urine, he will reach a stage in the dilution when the bead will cease to rise; and, after inverting the tube on the thumb, so as to secure a uniform mixture, it will either still fail to ascend, and will remain suspended at any part of the column—now of the same specific weight as that of the bead: or it may yet slowly rise; in which case, a little further dilution is needed to bring it to a stationary condition. When suspension of the bead has been thus secured, the figure on the *right* hand side which marks the height of the column, indicates the specific gravity: then the observer will find the bead is so delicately poised, that merely one drop of water will determine its fall.

If the bead still floats when the limit (1024) provided by the tube is reached, the diluted urine is poured out, or removed by the pipette, until the column stands at 24 on the *left* hand side; and water is added as before, and when the bead ceases to rise, the figure to the *left* expresses the specific gravity.

A little practice will soon enable the observer so to regulate the successive additions of water, as to determine the specific gravity with nicety without overstepping the limit; and in this he will be mainly guided by the rapidity or slowness of the rise of the bead projected downwards by each dilution—the slow ascent of course implying an approach to the point when the reading should be taken.[1]

[1] If the specific gravity is to be determined with accuracy a correction for temperature must be made; for all instruments are graduated at 60° F., and every 7 degrees of deviation from this temperature causes an error of one degree—to be subtracted from, or added to the registered figure according as the thermometer stands below or above 60°. To ensure this precision for observation at home, I use a urinometric arrangement made for me by Mr. Hawksley, 357, Oxford Street, consisting of a large bead (1005) and a graduated tube, fitted with a thermometer, which enables me to make the necessary correction at once. In frosty weather the observer will do well, in using the pocket tube and bead, to subtract 2°.

Advantages.—This mode of observation of the density of urine will serve the practitioner, not only on the score of portability, but in being helpful in furnishing reliable results under circumstances which prevent accurate determination by ordinary urinometers: as, for instance, when the sample of urine procurable is too small—as so frequently happens—or being recently voided, is so warm as to give, on immediate examination, a misleading density. In the latter case the requisite addition of water is a useful corrective.

The Clinical use of Specific Gravity.

The density of the urine provides useful clinical information as to the amount of solids discharged. It is a ready and time-saving quantitative method, which yields data sufficiently approximate to be useful in current clinical observation. Inasmuch as the urine passed at different times of the twenty-four hours varies very much in total contents—the specific gravity in the same individual often ranging from

1008 to 1028—the observer should, if possible, always take the density of the whole day's urine, and also note the quantity discharged.

The specific gravity of the twenty-four hours' urine may yield approximate information as to the daily amounts of total solids, of urea, and of sugar.

I. *The total solids, or 'solid urine.'*

A healthy man of from 20 to 40 years of age, and of about 10 stones (140 lb.) in weight, should excrete in the twenty-four hours as much urinary solids as will give a specific gravity of 1020 to 50 ounces of urine. If he discharges this average daily quantity of urine, it should contain a little over 4 *per cent.* of solids, or nearly 20 grains to the ounce; or in all about 1000 grains.

$$20 \text{ gr.} \times 50 \text{ oz.} = 1000.$$

The percentage of the solids oscillates from hour to hour, and from day to day, on either side of the mean (4 *p.c.*) and the specific gravity is in keeping with it.

When the specific gravity of the twenty-four hours' urine is lower than the average, the quantity is generally larger; and when higher, as a rule, the urine diminishes. So that in the calculation of the daily discharge of the urinary solids, the specific gravity alone, or the twenty-four hours' urine alone, is insufficient: they must be taken together.

The Rule for an Approximate Calculation.—A good and simple working rule is to multiply the last two figures of the specific gravity by the number of ounces of the urine: and the product will approximately represent in grains the 'solid urine' discharged in twenty-four hours. For example, sp. gr. 1019, urine 55 ounces:

$$19 \times 55 = 1045 \text{ grains.}^1$$

Before, however, comparing the solids thus calculated from data afforded by disease with the standard amount, the

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[1] A deduction of 5 *per cent.* provides a nearer approach to truth, *e.g.*

$$19 \times 55 = 1045 - 50 = 995$$

But the simplicity of the rule is thus somewhat impaired; and without this correction it suffices for all practical purposes.

observer should allow not less than one fifth, above or below it, as consistent with the variations of health. For example, the following urines fall well outside these limits.

(1) Specific gravity 1017: twenty-four hours' urine 40 oz.

$$17 \times 40 = 680.$$

(2) Specific gravity 1022: twenty-four hours' urine 70 oz.

$$22 \times 70 = 1540.$$

Physiological Causes of Variation.—On referring the estimations of the solids of particular urines to this standard (from 800 to 1200 grains) the observer, in order to qualify his opinion, should bear in mind the principal causes which determine the persistent excretion of different amounts of solid urine in the healthy; such as the following:

(1) *Food.* Meals always augment the solids; and the habit of full-feeding favours a permanent increase, and spare-eating the reverse.

(2) *Exercise and Rest.* An active life (physical and mental) tends to increase

the solids, while inactivity of body or mind disposes to a reduction.

(3) *Body-weight.* This is a leading cause of the individual variations in the daily amounts of urinary solids. The heavy, as a rule, excrete more than the light. Observation has shown that in adults each pound of the body-weight yields generally from 7 to 8 grains of solid urine, and, therefore, each stone (14lb) about 100 grains.[1] In woman an equivalent weight provides rather less urinary solids than in men. Children under seven years of age excrete in proportion to their weight, nearly twice as much solids as adults ; but, by the sixteenth to the eighteenth year, the relative amount settles down to that which obtains in after years.

In estimating the daily discharge of urinary solids, the qualifying influence of weight should always be taken into account—providing, however, that the patient is not too fat or bony : for fat and bone are tissues that contribute but little to the urinary excreta. The body-weight

[1] See *The Composition of the Urine* by E. A. Parker, M.D.

may sometimes decide the position of urines containing solids on the borders of the average amount, or may emphasize what appears to be the slighter departures. For example, when a man not unduly bony or fat, weighing 12 stones, is computed to eliminate 850 grains[1] (sp. gr. 1017 and urine 50 oz.) his urinary excretion may be said to be below par—for it is at least one third less than the amount (1200 grs.) calculated from his weight.

Clinical Variations. — The daily amount of solid urine is a valuable index of the tissue-changes—their rapidity or degree, and their disorder—and of the integrity of the kidneys. The morbid variations are such as fall below the physiological limits, or exceed them.

The Urinary Solids are deficient.

The urine itself may be normal in quantity, or it may be scanty, or excessive.

(*a*) *The amount of Urine is normal or subnormal.* — Without recognizable organic disease of the kidneys, or of other organs,

[1] Or corrected by deducting 5 *p.c.*—808.

the solid urine may be small, though the urinary flow is not reduced, or is only somewhat below the average. The habits of life may account for the failure, such as small eating, sedentariness, &c; or there may be a deficiency of muscular tissue—a tissue that yields a larger proportionate amount of urinary excreta than others; and, perhaps, a relative excess of bone and fat; or the defective excretion of urinary waste may indicate a slow and failing metamorphosis of tissue generally, as when nutrition is taking on the senile type prematurely, or when there is a lull in nutritive activity from some depressing influence. The condition described by Sir Andrew Clarke as 'renal inadequacy' is of this character, for it appears to be the expression of defective metabolism of the tissues rather than of renal failure. In forming an opinion of the reduction of the urinary excreta in such cases, the observer will bear in mind that after fifty years of age a gradual falling off takes place; a reduction of from 10 to 20 *per cent.* should be

allowed from fifty to sixty, and at least 25 or 30 *per cent.* after sixty. Then again, a fall in urinary solids marks the enfeebled metabolism in anæmia and hydræmia, and in the cachexia of syphilis, of cancer, and of chronic alcoholism. Imperfect action of the liver probably also reduces the solid urine, as when the hepatic function is merely debilitated or sluggish, or when there is organic disease, such as cancer, abscess, &c.

The elimination of solids is retarded when the kidneys are crippled by disease. In acute nephritis (as after scarlatina, &c.,) in the intercurrent inflammatory conditions of chronic renal disease, sometimes at the close of Bright's disease, and in hyperæmia of the kidneys (cardiac disease, emplysema dilating the right heart, &c.,) the urine itself is likewise reduced in quantity. In the early stage of renal disease, and even during the course of insidious chronic renal disease (as in the gouty and in the tubercular kidney) the daily amount of urine may be normal or sub-normal.

(*b*) *The Urine is increased in quantity.* The total solid constituents may be diminished while the flow of urine is excessive. This condition of persistent watery urine (hydræmia) is witnessed in diabetes insipidus, and in the cirrhotic kidney. In the waxy (amyloid) kidney, the discharge of the urine is also increased, but the daily elimination of the solids is not, as a rule, diminished.

The Urinary solids are increased.

As with the diminution, so with the increment of the solid urine, the discharge of the urine itself may not be augmented, or it may be excessive.

(*a*) *The amount of the urine is not increased.* In fever, as a rule, while the per centage of the total solids is raised, the total daily amount is not. But there may be an absolute as well as relative increase in certain forms of dyspepsia,[1] and in lithæmia.

[1] Dr. Fuller recorded this fact ("*On excess of urea in the urine in certain forms of dyspepsia and nervousness.*" Medico-Chirurg., Trans., Vol. 51, 1868.) in some cases of dyspepsia characterised by langour, inaptitude for exertion, extreme nervousness and apprehension, flatulence, acidity, &c., but without loss of flesh or of the appearance of health.

(*b*) *The urinary flow is excessive.* The augmented excretion of solids is usually accompanied by an increased discharge of urine: as in diabetes mellitus (persistent elimination of glucose in excessive quantity), phosphaturia (the 'phosphatic diabetes' of Tessier, in which the phosphates are thrown out in enormously increased proportion), and in azoturia (marked by excessive excretion of urea). Phosphatic diabetes and azoturia are rare forms of polyuria, which probably depend on augmented metabolism of the tissues from disturbed innervation.

II. *Urea.*

Urea forms very nearly one half of the total solids of healthy urine. In disease this proportion is sometimes considerably disturbed,[1] but not so frequently as might be supposed. I have now so often confirmed the *general* agreement, between the amount suggested by the specific gravity and that of the urea actually determined, that I have come to regard gravimetric observa-

[1] As in fever, diabetes mellitus, and renal disease.

tion as very useful, in providing at least a good approximation: and especially as suggesting in the preliminary enquiry the selection of particular urines for the ureometer.

It is pretty well known, that even when urea has been accurately determined, the observer is scarcely justified, as a rule, in concluding there is a decrease or an increase, unless the variation falls outside one-fifth of the standard mean—below or above it. Inasmuch, therefore, as the specific gravity will, in the absence of glucose, provide data that are, in a general way, commensurate with this wide margin of deviation, it should be of some use in contributing at least an approximation towards a reliable calculation of the amount of urea discharged—at any rate in the ordinary run of cases. The following examples taken from my case-book, illustrate the *general* agreement which usually obtains between the amount of urea calculated from the specific gravity, and that determined by the ureometer. The majority of the cases were renal.

Daily amount of urea in grains.

Calculated.	*Determined.*
320	301
300	259
205	210
184	197
586	597
440	444
445	431
460	470
368	344
360	340
507	525
451	497

The approximate calculation of the daily excretion of urea may be made by halving the total solids.[1] (See page 53.)

The Daily Average mean Amount Excreted.—Each stone of body-weight (apart from excess of fat or bone) yields

[1] The amount in *grains per ounce* may be estimated by subtracting the ratio of 1 degree in 10 from the specific gravity, then taking the last two figures and dividing them by 2, *e.g.*

1016—1.6=1014.4.

14.4÷2=7.2 grains per oz.

The *per centage* may be calculated by dividing the number of grains per ounce by 4.36, *e.g.*

7.2÷4.36=1.65.

about 50 grains. A healthy man, weight 10 stones, and age from 20 to 40, should excrete about 500 grains, with variations up to 100 grains, less or more. The total amount should be reduced by about 10 grains per stone in women, and should be doubled in children under seven years of age. A reduction should be made for age beyond forty; 5 *per cent.* from forty to fifty; and ten *per cent.* between fifty and sixty; and after sixty the decrease is proportionately greater.

The Chief Physiological Causes of Variation to be kept in mind are:—

(a) Increase from large eating, especially of nitrogenous (animal) food; copious drinking of water, particularly when warm; exercise, and full vigour and development of the muscles.

(b) Decrease from fasting or spare feeding, and the diet largely non-nitrogenous (starch and sugar) and vegetable; reduction or deprivation of water; alcoholic drinks (beer, strong wines) tea and coffee; indolence of mind and body, and lowered nutritive condition of the muscles.

The principal factors of the variations of urea in different individuals are *weight*, *diet*, and *work* (vital, mechanical, and mental). The causes of deviation in the individual — *diet* and *work* — continually present themselves to the clinical observer, who soon comes to estimate, in a general way, their influence. For example, when after prescribing a non-nitrogenous diet and rest to ease the renal work, he is careful to attribute the immediate fall in urea to the right cause—to his directions rather than to an increasing incompetency of the kidneys. By rest and diet the daily discharge of urea can be reduced by at least two-fifths, so that, for example, 500 grains excreted by a person taking ordinary exercise, will fall to about 300 grains, when he rests in bed, and takes merely such light food as will prevent waste of tissue. The diminished amount eliminated when the body is at rest, and preserved from loss of weight by a diet chiefly non-nitrogenous, nearly represents that portion of urea which is derived from the vital processes—about three-fifths of

the total discharge: the remainder—nearly two-fifths—being contributed by work.[1]

The Variations of Urea in Disease were for the most part sketched when the total solids were under review; for the causes that determine an increase (even in glycosuria) or a decrease of the solid urine, also produce a rise or fall in the amount of urea. This rule, however, fails in the case of fever, which augments the urea without increasing the urinary solids as a whole.

III. *Sugar.*

When the urine is glycosuric, there is generally a rise in the specific gravity above the normal range[2]: and, as a rule, the higher density is *in a general way* proportionate to the amount of sugar. Inasmuch as, in different cases, or even in the same case, there is no exact agreement between them, the specific gravity can

[1] See a very instructive essay *On the Natural Constants of the Urine of Man*, by the Rev. Prof. Haughton, F.R.S. Dublin.

[2] The exceptions to this rule should, however, be kept in mind; for occasionally a urine is met with containing sugar, though of average specific gravity.

only furnish a rough estimate: but it is one, nevertheless, that is suggestive in the preliminary enquiry. The principal source of the discrepancy is due to the varying proportions of the non-saccharine solids.

The Discharge of Urine exceeds 150 Ounces in Twenty-Four Hours.—When the urine is voided in large quantity (*e.g.* over 150 oz. in twenty-four hours) the precentage of the urinary solids falls to such an insignificant degree, that the secretion is practically little more than a solution of glucose, and the specific gravity becomes a fairly accurate guage of the amount of sugar—each degree over the thousand being nearly equivalent to one grain per ounce.[1]

The Daily Flow of Urine is under 150 Ounces.—When the discharge of urine is less copious, the variations between the specific gravity and the amount of sugar become very considerable. For example: eight cases of

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[1] Experiment shows that the last two figures of the specific gravity of a solution of glucose nearly correspond fairly well with the number of grains per ounce: *e.g.* a 5 *per cent.* solution (21.8 grains per ounce) gives 1021.

excessive flow (over 150 ounces) with an average specific gravity of 1041, eliminated 42 grains of glucose to the ounce; and ten cases, in which the discharge of urine was less, with an average density of 1035 excreted only 25 grains per ounce.

When the daily amount of the urine is below 150 ounces, an average deduction for non-saccharine solids may, however, be made, which considerably reduces the discrepancy between the specific gravity and the amount of glucose. The rule for this correction is—to subtract from 1020, 1 degree for every 5 ounces of urine over the average discharge of 50 oz. (see p. 44); and then to deduct the figure thus obtained from the specific gravity of the urine; when the remainder will roughly represent the glucose in grains per ounce: for example, urine 90 ounces, specific gravity 1039;

1020—8 (5×8=40 oz. over 50)=1012.

1039—1012=27 grains per ounce.

It is true the quantity thus calculated is but a general approximation: but even as

such it may be sometimes useful; as when the busy practitioner cannot avail himself of one of the accurate quantitative methods.

IV. *The Specific Gravity of isolated specimens of Urine.*

When the twenty-four hours' urine is not available, and observation must be made on isolated samples, the specific gravity may still be clinically useful: providing the observer is on his guard against the principal disturbing influences —notably meals and sleep.

Maximum Solid Urine.—He will specially bear in mind, that the urine contains its maximum charge of solids from three to four hours after a meal; when it, therefore, attains its highest range of specific gravity, from 1020 to even 1027, *e.g.*, from 12 to 1 when breakfast is taken at 8-30 or 9, and from 5 to 6 when the patient dines at 2. This physiological fact tells on the clinical conclusions to be drawn from the urine in two ways. In the first place, a falling off of the specific

gravity below 1020 at these periods—when it should reach its maxima—affords greater presumptive evidence of renal failure—especially when albumin is present in even small quantity—than does the urine voided at other times. And, secondly, if the specific gravity is high, the detection of traces of albumin, &c., is of somewhat less clinical significance than when it is low or below the normal mean; allowance should, therefore, be made for the concentrated condition of the urine.

Minimum Solid Urine.—On the other hand, the observer requires to be cautious in drawing conclusions from his examination of urines voided at times, when the least proportions of solids are discharged: as for example, during the night, and on rising;[1] an hour or so after a copious draught; and when the patient is nervous and flurried by the medical enquiry into his case, or by some other cause. Then

[1] The urine of a person in health passed either during the night, or on rising, contains, as a rule, but one half of the solids discharged four hours after a full meal—breakfast or dinner—and especially the latter.

the specific gravity is low, and no clinical significance can be attached to it on that account. But the observer will bear in mind that the discovery of a trace of albumin, bile-salts, &c., in a urine of small density—*e.g.*, 1008 or 1010—is, as a rule, more suggestive of something wrong, than when a similar minimal quantity is detected in a more concentrated urine; and it should then direct the clinical enquiry towards the kidneys, liver, &c. The observer should remember there is one property of the urine which does not maintain a uniform relation with the different degrees of concentration, viz., the reaction; for when there is a maximum of solid urine—four hours after a meal—there is a minimum acidity, and when the solids are reduced, as during the night and before breakfast, the acidity is increased (see p. 75).

Practical inferences.—Bearing these facts in mind, the observer, confined to the examination of isolated samples of urine, will draw the following conclusions :—

(a) He will select, if possible, the most concentrated specimen—that voided four hours after a full meal—as well as that passed before breakfast; and he will not rely solely on the latter.

(b) In comparing the results of treatment, he will submit to examination, as far as practicable, only such samples as are of similar specific gravity, and discharged at the same hour.

CHAPTER III.

THE REACTION OF THE URINE.

Modes of determining the reaction.

Litmus papers.—Blue and red litmus papers—the former for determining acidity and the latter for alkalinity—have been found the most convenient for all clinical purposes. Litmus of neutral tint—serving for both acidity and alkalinity—is unfortunately apt to pass from exposure into the red variety. The degrees of acidity or of alkalinity are generally judged by the slightness or sharpness of the change of colour, and a neutral reaction does not affect either test-paper.

Red litmus paper not only detects alkalescence, but it enables the observer to distinguish when the alkalinity is due to a fixed alkali (potash or soda), or to the

volatile one (ammonia): for, in the former case the blue colour remains after the paper has been thoroughly dried, while in the latter it vanishes.

Alkalinized Litmus Paper.—Ordinary blue litmus paper, while deciding definitely enough whether a urine is acid or not, provides but the most general evidence of the various degrees of acidity: for, nearly all urines—though differing greatly in respect to their charge of free acid and of acid salts—react with it very much alike. Clinical requirements frequently demand a definite scale of acidities—in the place of the loose general impressions afforded by simple litmus paper—and I find that such can be provided, by charging test-papers with a uniform quantity of alkali—carbonate of soda—along with the litmus. These alkalinized litmus test-papers have afforded me very satisfactory and definite results, and I recommend the following as the best mode of using them.

One of the test-papers is dropped into 60m of water; after a little vigorous

shaking with the thumb over the mouth of the tube, a blue emulsion is produced; into this urine, in stages of 10m at a time, is run; and after each addition the contents of the tube are shaken up. The reaction is at an end, when the blue colour acquires a reddish tinge— a transition tint: then it will be definitely replaced by red, on adding a further 10m of the urine.

Degrees of Acidity.—This mode of observation enables the practitioner to recognize definitely four degrees of acidity; namely:

Super-acid,	when	10m	of the urine	are required.
Per-acid,	,,	20m	,,	,,
Acid,	,,	30m	,,	,,
Sub-acid,	,,	40m	,,	,,

For example: when the urine has an average degree of acidity, the addition of the first and of the second 10m merely reduces, and does not tinge by red the blue colour; but on adding the third 10m a reddish blue tint appears; and 10m more strike up a distinct red colour.[1]

[1] Artificial light is not favourable for the observation of these colour reactions.

This method is ready and practical; and it certainly provides more precise and useful results than can be obtained from ordinary litmus paper.

Physiological Variations of Reaction.

During the twenty-four hours the urine undergoes a remarkable series of fluctuations in its reaction. The normal urine of the whole day provides a mean of acidity, which at certain periods is greatly exalted, and at others depressed: it is raised before meals, and during the hours of sleep; and is lowered for several hours by feeding. Even in health the urine may become neutral, or even quite alkaline two or three hours after meals. The wave of reduced acidity that follows the meals has been aptly termed the 'alkaline tide': which generally sets in an hour after breakfast and two hours after dinner, retaining its maximum strength[1] for an

[1] In most urines the 'height' of the alkaline tide is marked by milkiness of the urine when voided—the earthy phosphates falling out of solution from deficiency of acid: the urine being either sub-acid, neutral, or alkaline. This occurs more particularly three or four hours after the largest meal of the day, *e.g.*, after dinner rather than after breakfast.

hour in the former case, and for at least two hours in the latter, and then turns, and is replaced by the 'acid wave,' which either immediately precedes the following meal,[1] or developes during the interval of fasting and rest. (See diagram.)

The 'acid wave' that follows the 'alkaline tide' is in proportion to the intensity of the latter: in other words, the wave of depressed acidity is remotely followed by a corresponding wave of exalted acidity. Animal food has a greater power to increase this remote effect than vegetable food.

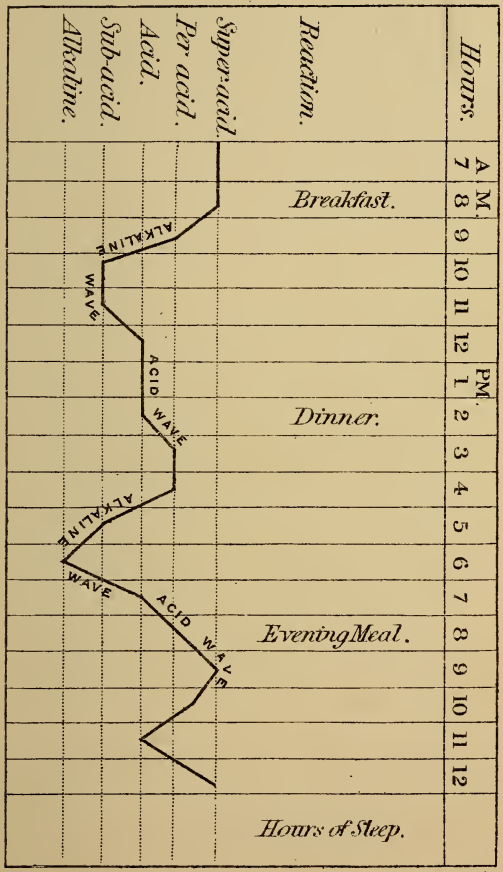
Clinical Significance of the Reaction.

In disease we are mainly concerned with high acidity and with alkalinity.

Urines highly acid.—Whatever concentrates the urine increases the acidity (see p. 59). Hence a febrile movement attended by perspiration raises the acidity: *e.g.*, rheumatic fever. In dys-

[1] I have repeatedly observed, that the degrees of acidity noted before dinner (at 2 p.m.) and evening meal (at 8), *increase* for an hour or so after these meals: but I have not detected the same fact after breakfast. (See diagram.)

The hourly fluctuations of the reaction of the Urine as determined by the Alkalinized Litmus Paper.



pepsia—especially of the acid type—the urine is frequently highly acid, while at other times it is neutral or even alkaline; this variability of the reaction is a marked feature in all derangements of the digestive organs—and is even more pronounced in children than in adults.[1] In diabetes mellitus the urine is generally per-acid.

Per-acid, and especially super-acid urines deposit urates as they cool—even sometimes this will happen at the moment they are discharged into a cold vessel. A urine may, however, be per-acid, or even super-acid, though remaining transparent in the cold. The observer should bear in mind, that the urine voided before breakfast, is generally more acid than that passed at other times. The sense of smell sometimes suggests the presence of an excess of acid.

Inasmuch as the higher ranges of the acidity of the urine are, in all probability,

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[1] In these cases, just as the reaction alternates from decided acidity to alkalinity, so the nature of the deposits varies: the acid samples becoming turbid from amorphous urates, and letting fall crystals of uric acid, while the alkaline ones are milky from earthy phosphates.

salutary, in being one of the principal channels by which the due alkalinity of the blood is maintained, the practitioner should test the strength and duration of the acid tides, whenever there is a disposition to the development of diseases depending on sub-alkalinity: such as rheumatism and gout; and, should he detect a failure in the acid waves, either in intensity, or in the time they should run, he may take the hint which physiology affords, and widen the intervals between the meals. The best urines for determining this matter are those passed in the early morning, immediately before dinner, and within two hours afterwards: and the observer will bear in mind that the first should be super-acid, the second acid, and the third per-acid.

Urines Alkaline.—Alkalinity is due either to a salt of a fixed alkali (carbonate or phosphate of potash or soda), or to the carbonate of the volatile alkali—ammonia. I have already referred to the distinctive odours of the two kinds of alkaline urine (see p. 19): and the different reactions

with red litmus—fixed in the one case, and fugitive in the other (see p. 72). Fresh urine, alkaline from fixed alkalis, is always secreted as such—and is, therefore, the expression of the blood-state—and does not irritate the mucous membrance of the urinary passages: but, on the other hand, that which is ammoniacal, is scarcely ever—if ever—furnished in that condition by the kidneys, but is derived from decomposition of urea in the bladder, and is, moreover, most irritant to the mucous lining. All alkaline urines are turbid from the precipitation of earthy phosphates; and often from pus.

Alkalinity of the urine from *fixed alkalis* is often found, whenever there is general debility and anæmia from almost any cause: when bile-derivatives pass freely into the blood: and when there is dyspepsia in which acid fermentation is a prominent feature.

Urine *ammoniacal when voided*, is generally associated with cystitis, and, therefore, with all the causes of this disease.

CHAPTER IV.

THE FORMS OF PROTEID SUBSTANCE IN THE URINE.

The properties of albuminous matter in the urine vary according to its chemical form and combination. Different proteid bodies have been isolated and studied; but they are all closely allied as members of the same family group.

Heat divides them into two classes, according as it does, or does not, coagulate them. Those that are precipitated by heat are the 'native' proteids of the blood—*i.e.* natural to the blood; *serum-albumin* and *globulin*. Those that are unaffected by heat, are 'derived' proteids —*i.e.* transformations of the 'native' proteids; such as the *albuminates*—combinations of albumin with an acid or an alkali—*peptones* and *hemi-albumose*.

Class I. Native Proteids.

Coagulable by heat: the coagulum being permanent at the boiling point.

(*a*) **Serum-albumin.**—From the clinical stand-point serum-albumin is the most important proteid that appears in the urine. It is necessary that we should be able to definitely determine its presence or absence; and, when present, to distinguish it from all other modifications of albumin, which indeed are met with but seldom, and which occupy a clinical position quite subsidiary. The modes of bedside testing, which appear to me to reliably secure this aim, and an outline of the clinical bearings of serum-albumin in the urine are reserved for Chapters v., vi., and vii.

(*b*) **Globulin.**—The globulin of the blood-serum is chemically allied to serum-albumin, and when it appears in the urine —as it frequently does—it is always, or nearly always,[1] associated with albumin. Heat cannot distinguish it from serum-

[1] Werner reports a case of nephritis, due to cold in a boy of 5½ years, in which the urine contained globulin only (*Deutsche Med. Wochensch Band* 46, 1883).

albumin, for it coagulates both: and it is equally affected by other albumin precipitants. But it differs from albumin in being insoluble in pure water, or in water containing salt in less than a certain small proportion—though soluble enough in the urine which is sufficiently saline. When, therefore, the salinity of a urine, containing globulin in quantity, is reduced by diluting it largely with water, the globulin falls out of solution, and furnishes a milky appearance. This fact provides a ready clinical test for detecting this proteid in albuminous urine.[1] The milkiness of the globulin-reaction with water vanishes on dropping into it either a citric or a soda test-paper. When globulin is dissolved in a slight excess of an acid, or of an alkali, it is at once converted into acid-albumin, or alkali-albumin respectively: and it is one of the probable sources of these forms of albumin in the urine.

[1] This observation can, of course, only be made properly, when the urine is perfectly transparent: so that filtration should be resorted to if there is any opacity. The urine may either be dropped into the water contained in the test tube, or about 20m of the urine are gradually diluted until the milkiness appears.

Globulin has been frequently detected in acute nephritis, and in Bright's disease —in the early acute stage (blood in the urine), and in advanced renal disease, when the patient has become very anæmic. It is most abundant in waxy kidney (Senator). It is said to be freely present in catarrh of the bladder.[1]

Class II. Derived Proteids.

Non-coagulable by heat; or, if coagulable at a certain temperature, completely clearing up below the boiling point—the vanishing precipitate reappearing as a diffused opacity as the urine cools (hemi-albumose).

(*a*) **Albuminates.** — Albumin readily combines with an acid or an alkali, and the definite compounds thus formed are no longer coagulable by heat. The urine not unfrequently presents conditions which favour such combinations, such as the presence of a fixed alkali, or an unusual charge of free acid, *e.g.*, lactic, oxalic,

[1] *A Guide to the Practical Examination of the Urine*, by James Tyson, M.D., 1884, p. 47.

acetic. The reader will call to mind, that of the blood-derived albumins, globulin is very prone to pass into the form of an acid, or an alkaline albuminate.

Though acid and alkali-albumin are not as such precipitated by heat—which may, therefore, overlook them—when the former is converted into ordinary albumin by an alkali, and the latter by an acid, coagulation at once takes place. To ensure this result, neutralization is best effected in the following manner, by the acid and alkaline test-papers: the urine is boiled, and while hot, a test-paper (citric for alkali-albumin, and soda for acid-albumin) is dropped in, when a streak of albuminous opacity will follow the paper as it sinks to the bottom.

Both these modifications of albumin are thrown down by the ferrocyanic and mercuric test-papers, and the precipitate of the latter does not dissolve up with heat, as does that derived from peptones. Therefore, in a urine unaffected by heat, a precipitate, insoluble with heat, induced by

the mercuric test-paper—or by a solution provided by it — suggests one of the modified albumins—acid-albumin or syntonin, or alkali-albumin or casein.[1]

(*b*) **Peptones.**—In 1852[2] Mialhe asserted that digested albumin (the peptone of Lehmann) may appear in the urine; and since then the observation has been confirmed by several trustworthy clinical observers. Chemists have distinguished several forms of the soluble and diffusible proteids which pass under the generic term 'peptones': but little is known as to whether one or several varieties of them may be met with in the urine.

Several well defined chemical properties separate these 'peptoid' bodies as a family group from the blood-derived albumins—globulin and serum-albumin; such as :—

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1 In testing for albumin by heat, acid and alkaline albumin may be unwittingly produced by the impurity of the test tube—as when a small quantity of nitric acid, or of Fehling's solution remains after using these reagents, then the heat test may completely fail in precipitating albumin, even though present in large quantity.

2 *L'Union Médicale*, 1852.

(1) Non-precipitation by heat,[1] or by the ferrocyanic test-paper.[2]

(2) Precipitation by the mercuric test-paper: the precipitate dissolving with heat, and re-appearing as a diffused opacity as the urine cools—no longer falling into coagula in the cold; and, on re-heating, vanishing again, without breaking up into coagula, as on the first application of heat.[3]

Inasmuch as peptone often appears in the urine along with serum-albumin, it is clinically important to know how to readily distinguish between the two bodies occurring together. I find the following

[1] The body called *hemi-albumose*, identified as the peculiar form of albumin discovered by Bence Jones in a case of osteo-malacia, is however, partialiy coagulated by heat, but the opacity vanishes as the temperature is further raised, and re-appears as the urine cools. The properties of this proteid point to its being a transition product between albumin and peptone. It is precepitated by the ferrocyanic test.

[2] I have observed that a peptone, added to urine, or to a solution of salt, is not precipitated by the ferrocyanic test-paper; but, when merely dissolved in water, it is freely precipitated. This fact may account for the opposing statements of observers in reference to the behaviour of this test with peptones. It does not precipitate them in urine. (Senator).

[3] I find that heat does not clear up the precipitate induced by the mercuric test-paper, or by the picric solution, when the peptone is dissolved merely in water; but it does so on adding salt; the presence of the salt in urine is, therefore, necessary for the complete removal of the opacity.

a good and easy procedure in the preliminary search :—

The proteid matter contained in 60 minims of urine is precipitated by the mercuric test-paper—two reagent papers being used if the amount of albuminous matter be pretty large. On applying heat, the opacity gathers up into dense coagula, which mass together, and either float up bodily like clotted cream to the surface, or fall ; leaving the urine transparent, or only slightly opaque, from a trace of albumin that will not coagulate by heat. After boiling, the test tube is filled with warm water to slight overflowing, so as to float out the scum of coagulated albumin, and, after adding a pinch of salt, is set aside. In the course of five minutes the larger particles and coagula will have subsided, leaving the column merely milky. The upper inch is now boiled, so as to test whether the opacity be due solely to albumin, or to albumin along with a peptoid body ; for, if it remains unimpaired, it is due to a blood-derived

albumin, but if the portion heated becomes decidedly less opaque than that below it, or if it clears up entirely, the presence of the soluble form of albumin may be strongly suspected; and if, after the addition of another reagent paper—so as to be quite certain there is an excess of the reagent over the amount of blood-derived albumin present—the opacity still diminishes or vanishes with heat, the presence of peptone will be confirmed by other tests.[1]

[1] According to my observation the best confirmatory test is the cupric.

The Cupric test for peptone.—Add a drop of a solution of copper to one dram of the suspected urine, and then one dram of liq. potassæ. If the urine be free from albumin or peptone the caustic potash merely intensifies the blue colour induced by the salt of copper; if, however, albumin be present, the solution will assume a browny-red colour; if peptone, a rich purple tint; and if albumin and peptone, a reddish purple.

Dr. Ralfe prefers the cupric test in the form of Fehling's solution. He floats a layer of the suspected urine on the test solution; where the two fluids meet a zone of phosphates is deposited, and above it a coloured halo developes—rose or pink tinted if peptones are present, mauve if albumin, and violet if much albumin with peptones.

Dr. Archer Randolph, of Philadelphia, suggests Millon's reagent with potassium iodide (see the *Lancet*, June 28th, 1884,) as a test for peptonuria. Two drops of the reagent are added to 60m of urine containing one drop of a saturated solution of potassium iodide; when a *yellow* precipitate falls, instead of a *red* one, in the presence of peptones or bile-acids, even in so small a proportion as 1 in 17,000. The clinical value of this test—which is indeed very delicate—is, however,

The Clinical Significance of Peptonuria.

Those[1] who have worked at peptonuria, and have, therefore, had special and large experience, are distinctly of opinion that it is always a morbid fact: and one, moreover, independent of albuminuria—for they found large quantities of peptones in the urine without a trace of albumin, and albumin without peptones.[2]

Peptonuria has been detected in various local and general diseases; such as the following:—

(1) *Local inflammatory affections:* especially those tending to the formation of pus. Not, however, in all local inflammations, even when suppurative, does peptonuria occur; for it is often absent in the chronic forms. Though it is not a positively differentiating sign between simple and purulent exudation, it affords, in

somewhat impaired by its failing to afford in undiluted urine quantitative information—the reaction being about the same with mere traces as with large quantities—and by the fact that bile-acids, which react the same as peptones, are often met with in excess. (See p. 204).

1 Such as Frerichs, Schultzen, Reiss, Hofmeister, Maixner, Jaksch, Poehl, Gerhart, Eichwald, Petri, and Obermüller.

2 In some of Gerhart's cases peptonuria, however, preceded albuminuria.

obscure cases of local disease, great probability in favour of the existence of an inflammation of a suppurative character, rather than that of any other morbid state. In malignant new growths of rapid development there may be, though rarely, peptonuria. In nephritis—acute and subacute, but especially in acute—peptones have been found (Eichwald).

(2) *In lobar pneumonia—especially in the period of resolution—and in pleurisy*[1] peptonuria is very frequently met with. In pneumonia it has also been found before resolution occurs, or in the course of grey hepatization; but less often than during resolution.

In twelve cases of acute rheumatic effusion Jaksch found peptonuria in all. Peptones are apt to appear in the urine when exudations (purulent, &c.) are absorbed in any part.

(3) *In general diseases (infective or not)* peptonuria has been detected; such as in diphtheria, malarial fever, typhus, typhoid

[1] Peptonuria was detected twenty-four times out of twenty-six cases of croupous pneumonia, and in four out of five cases of pleurisy. (Jacksch, quoted by Dr. Ralfe.)

fever, small-pox, cerebro-spinal meningitis, scurvy, purpura hæmorrhagica, septicæmia, tertiary syphilis, and acute phosphorus poisoning. In these cases it is sometimes indicative of profound disturbance; as when there exists a very high temperature and adynamia in scurvy, purpura, malaria, and typhoid: but it is not always expressive of the intensity of the ailment, as it has been found in certain cases of slight sub-continuous miasmatic fevers.[1]

(4) *Disorders of the liver.*—I think there is some probability in the view, that peptones, generated by the digestion of proteids in the stomach and duodenum, may, in certain cases of failure in the construction of glycogen, pass through the liver into the general circulation, and then—being much more diffusible than the albumin of the blood—they will readily dialize through the renal glomeruli, and appear in the urine. In such instances, the presence of a peptone in the

[1] See Dr. Petri's paper on peptonuria in *Annali Unio. di Med.*, Aug., 1884.

urine will be of like clinical significance to that of glucose, when glycosuria indicates some hitch in the constructive assimilation of the products of digestion by the liver. But the appearance of peptones in the urine, indicative of a hepatic defect, may only be a comparatively rare event; for, there is some reason for the belief, that the blood and the tissues have the power to assimilate them — probably by dehydration[1] converting them into other forms of proteid. If this be so, it merely reduces somewhat, and does not obviate the liability of peptones to pass out by the kidneys: for the failure of the liver to fix these diffusible proteids may be shared by all the tissues. The frequency of peptonuria in malarial disorders—whether accompanied by high temperature or otherwise—which so frequently disturb liver-work, and in profound febrile action generally, in which the metabolism of the

1 Peptone appears to be chemically related to albumin in much the same way as glucose is to starch, namely, in being a hydrate, or albumin *plus* water, as glucose is starch *plus* water.

liver and of the tissues is very active and greatly disordered, appears to me to suggest the hepatic origin of peptonuria; and the two cases of temporary albuminuria and peptonuria referred to by Dr. Ralfe, and several observations of my own in the same direction, undoubtedly support it. I am, therefore, disposed to place peptonuria (temporary, or intermittent, or minimal though it be) by the side of minimal glycosuria and the bile-salts (see chap. xiii.), as affording the most reliable clinical evidence, provided by the urine, of imperfect or perverted liver-work. Then again, I am disposed to think that now and then peptones in small quantity appear in the urine—especially an hour or two after dinner or the heaviest nitrogenous meal—as a result of an excessive flow of them to the liver: the diet being too rich in proteids.[1] Dr. Lauder Brunton, in his light-giving Lettsomian lectures on

[1] There is, however, some ground for believing that, as a rule, an ingestion of proteids beyond the requirements of the system is largely got rid of by tryptic decomposition: pancreatin having the power to split up peptone into lencin and tyrosin. Still this process of destruction may not obviate in all cases a too free supply of peptones to the liver.

'*Disorders of Digestion: their consequences and treatment*,' just delivered, touches with much point on the ill consequences of this fact, when he says: "many a man has been saved by a weak stomach, which punished its owner by sickness or headache whenever he tried to over-burden it, and thus checked his tendency towards excess at the very outset. Where the stomach and intestines are more accommodating, and continue to digest all that is put into them, the burden of the work is shifted elsewhere, and either the liver fails to reconstruct the new material with which it is deluged, or the tissues are poisoned, and the over-worked kidneys become degenerated." And again: "If these products of digestion be absorbed in large quantity, and pass too rapidly through the liver, so that they reach the general circulation without undergoing sufficient elaboration, they will either prove injurious to the organism, or be excreted as waste products, or both. Indeed, we find this to be the case, for we frequently meet with affections of the respiration, circulation,

and nervous system, which actually seem to be due to a kind of poisoning by products formed, either in the intestinal canal itself, or in the blood; and we also meet with cases in which sugar, peptones, and albumin are excreted by the kidneys, instead of being applied to the repair of the tissues. . . . . Clinical experience had indicated a connection between long continued digestive disturbance and organic disease of the kidneys, and this was experimentally demonstrated by Stokvis, who found that hemi-albumose (see p. 88) injected under the skin once or twice, will pass out through the kidneys without doing them any apparent injury, but if the injections be frequently repeated, the hemi-albumose, in passing through the kidneys, appears to excite in them organic disease."

According to my observations, the conditions that prevent precipitation of proteids in the duodenum—viz., an excess of the proteid, or a deficiency or excess of bile, or of acidity—may induce the premature absorption of them. (See p. 206).

CHAPTER V.

ALBUMINURIA: THE DETECTION OF ALBUMIN BY ACIDULATION (CITRIC ACID TEST-PAPER) AND HEAT.

Different modes of applying the test of acidulation and heat. — If I take an albuminous urine of normal acid reaction: boil it thoroughly: and then add an organic acid—citric or acetic: and filter: I obtain a filtrate, which, according to the picric acid solution, or the mercuric test-paper, contains a small quantity of albumin—for the opacity induced by the tests does not vanish in either case with heat. But if, before boiling, I add a citric acid test-paper, or a drop of acetic acid to a four inch column

of the urine, the filtrate, as a rule, contains the very merest trace of albumin.[1]

I, therefore, conclude that boiling *before* acidulation is a less sensitive albumin-test than the mercuric and the picric: and, furthermore, than boiling *after* acidulating the urine to the proper degree[2]—a proceeding which precipitates virtually the whole of the albumin.

Boiling after acidulation.

Preliminaries.—In applying the heat

[1] I find by experiment, that if albuminous urine is acidulated as above, is thoroughly boiled, is further acidified by two or three drops of acetic acid, and re-boiled, the filtrate does not contain a trace of albumin—so far as can be ascertained by any direct testing. I, therefore, regard this as the most sensitive mode of applying heat. Its searchingness is shown by the fact, that according to my observations with it during the past few months, it has demonstrated the presence of albumin in all healthy urines of specific gravity 1020 or over —of course a mere trace in most, but still distinctly recognizable on shading the tube with a dark back ground. With normal urines of lower specific gravity (e.g., 1015 or 1016) the presence of albumin cannot be shown in all cases by this mode of applying the heat test. I daily meet with normal urines, which, though affording no reaction after acidulating (by one drop of acetic acid, or by a citric test-paper) a four inch column in a $\frac{5}{8}$ inch test tube and boiling, develop a haze in the upper boiled portion in a few seconds, after adding a drop or two of the acid, or another citric test-paper *immediately following* the first boiling; and the delicate reaction thus obtained, is somewhat increased by the further application of the lamp—the urine being kept on the simmer for a minute.

[2] This mode of applying the boiling test was introduced by Dr. Wm. Roberts, *op., cit.*

test after acidifying the urine, the reaction should first be taken; if alkaline or neutral, the urine should be acidified slightly, or up to the supposed normal degree, before the observer adds the standard quantity of acid; but, if normally acid, no such rectification is required. If the urine be per-acid—as indicated, for example, by the deposition of urates—though there are many per-acid urines free from such deposits—boiling may proceed without any preliminary acidification. But in any case the observer requires to be always on his guard, lest he should unwarily create a pitfall by over-stepping, even only slightly, the required degree of acidity: for, then he will prevent the coagulation of even a large quantity of albumin; this may easily occur, if he overlooks the per-acid state of a urine, and in a routine way, adds the quantum of acid, determined by experience as the best, when the urine is normally acid prior to testing.

The Method.—The most convenient way of acidifying and boiling for bedside

observation is: to fill the test tube with the urine up to the topmost mark; to add half a citric test-paper[1]—after acidifying to the normal degree alkaline or neutral urine with small pieces of the same paper; and then to boil the upper half of the column. Any opacity that appears is albumin, and nothing but albumin.

Objection.—According to my observations this mode of testing is undoubtedly open to the objection that has been urged against albumin-precipitants more delicate than nitric acid: that for clinical purposes they go too far, and include within their range a very large number of healthy urines containing albumin in small quantity; thus, either necessitating an enquiry into the source of the proteid in each case—a proceeding that must consume more time than can be afforded by most observers—or leaving the practitioner in doubt as to the clinical importance, if any, of the minimal proportions

[1] The acidity of one citric test-paper is that of one and a half drops of acetic acid (B.P.). Hence half a paper in 2 drams of urine is equivalent to one drop of acetic acid in 3 drams—the proportion advised by Dr. Wm. Roberts. *Op. cit.*, p. 186.

of albumin thus brought to light. Should the observer carefully apply the heat test after proper acidulation — using either acetic or citric acid, for both give the same results—to a series of urines, he will, I think, be somewhat astonished to find what a large proportion of healthy urines—or rather of urines of healthy people—contain a trace of albumin : the merest trace, it is true, in many—but just sufficient to enable anyone to decide that they are not chemically free from albumin. I have carefully and repeatedly watched, by the heat test with previous acidulation, the temporary appearance of small quantities, or traces, of albumin in urines generally regarded as albumin-free —though not absolutely so—due to transitory hygienic, dietetic, or climatic influences, such as a slight biliary disturbance, a little indigestion, chilling, meteorological impressions, cold bathing, &c. Surely these and many other similar conditions of life must affect every one, less or more, and thus induce the appearance in the urine of the traces of albumin

so frequently met with. It *may* be true that a perfectly normal urine is, so far as can be ascertained by direct testing, absolutely albumin-free: but I am persuaded, that the attribute of normality which this dictum implies, does not apply to the majority of healthy persons.

An Albumin Test required of Intermediate Detecting Power between Nitric Acid and Heat with Acidulation.—Nitric acid falls far short of heat as a sensitive test. If the observer will take an albuminous urine, dilute it with albumin-free urine, until nitric acid, when run below it after the 'contact' method, fails to give an immediate indication of the presence of albumin, but one, nevertheless, that develops as a delicate zone in the course of a minute: he will find that, after several further dilutions with albumin-free urine, or with brine, acidulation and boiling will distinctly detect the albumin —and even when diluted five-fold, a haze will still be apparent. Hence, I conclude, that nitric acid is an albumin test at least

five times less delicate than acidulation and boiling. And this position, furthermore, agrees with clinical observation. Repeatedly during the past few years nitric acid has afforded me negative evidence of albumin, or has indicated mere traces, when heat and other tests have shown the pressure of definite quantities, the detection of which was a matter of some clinical importance and interest. It would therefore appear, that for clinical purposes, nitric acid is as insufficiently acute, as acidulation and boiling, and other tests of similar delicacy, are too sensitive; for, in using always the former the observer occasionally runs the risk of over-looking pathological albumin, and in employing the latter, in the same routine way, he is apt to be confused by physiological albumin–or by the transitory traces of albumin determined by conditions of little or no clinical importance. What is, therefore, needed as most useful for all ordinary observation, is a reliable test of intermediate power, or as Dr. Wm. Roberts says, "It is no doubt

desirable that we should possess a test for albumin, somewhat more sensitive than nitric acid, but it is a condition, *sine quâ non*, that such a test shall be equally reliable."[1]

As I will show presently, the albumin precipitants I use for bedside purposes, when employed in a definite manner, provide three ranges of power: that of nitric acid, that of acidulation and boiling, and that of an intermediate degree; and, moreo er, the reliability of the tests is increased, if not ensured, by the improved mode of applying them.

Acidulating after boiling.

If the observer prefers to employ heat in the ordinary way, he should boil the upper half of the column of urine, and if any opalescence appears, he should insert into it a citric paper; then, if the opacity vanishes with effervescence, it is due to phosphates, and any turbidity that remains arises from coagulated albumin.

Heat not necessary as a routine Preliminary Test.—Boiling along with

[1] *Op. cit.* P. 189.

acidulation will always maintain its position as an albumin test. But I am satisfied it is not a necessary condition of safe clinical observation to always resort to it in order to answer the routine preliminary enquiry—is the urine albuminous or not? As every one knows, it is only here and there in the ordinary course of work, that albumin of clinical significance is met with; and when, as in the great majority of the samples of urines tested, the handier tests give no indications, the observer may rest satisfied that boiling will be equally negative, and the enquiry is at an end; and in the comparatively few cases in which they do afford indications of the presence of albumin, the practitioner may, if he so wish, verify the result by the boiling test; but a little experience will soon show him that this appeal is but rarely necessary.

As a rule heat is selected over other tests when a urine is loaded with lithates, because it is generally necessary to first of all clear these away with warmth, and then it is a simple matter to carry the

heating forward to boiling; and, furthermore, such a urine is always sufficiently acid for albumin testing by heat. But this condition does not lead me to select heat as the preliminary test; for, the procedure I adopt does not require the urates either to be cleared up by heat, or to be filtered out.

Then again, an opacity due to earthy phosphates is clarified by the acidulation prior to boiling: but this does not constitute a preference for heat; for, in the cold mode of testing presently to be described, the phosphatic turbidity vanishes as readily as does the dense cloud of urates.

If a urine is turbid from organic causes —pus, blood, &c.,—it should be filtered; but if this is impracticable, or a clear sample derived from subsidence cannot be obtained, heat is preferable as the preliminary test.

The modes of Heating.—At the bedside cleanly heating and boiling are best effected by either of the following ways:—

(a) A long wax match, or taper, or candle; the tube being always held clear of the tip of the flame, when smoking of the glass will be entirely avoided. A little practice will enable the observer to boil by these simple means in as smokeless a manner as by the spirit lamp.

(*b*) Neat little spirit lamps provided by the instrument makers.

CHAPTER VI.

ALBUMINURIA: THE DETECTION OF ALBUMIN BY TEST-PAPERS.

The Test-Papers Selected.—Of the series of albumin-precipitant test-papers, which some two years ago, I brought under the notice of the profession, I am led, as the result of observation, to select two—they being, in my opinion, the most generally useful and trustworthy in the preliminary search for albumin in the urine: namely, the potassio-mercuric iodide, and the potassium ferrocyanide, which, for the sake of brevity, I will designate the 'mercuric' and the 'ferrocyanic' test-papers. The test in each case consists of two papers: one charged with the reagent; and the other with citric acid.[1]

[1] I think it is best to apply the acid and the reagent papers separately: they are, however, combined by a thin layer of rubber in the *compound* mercuric test-paper, which, from its simplicity as a single paper, is preferred by many practitioners.

Mucin.—Exception having been made to the albumin test-papers, when employed in determining small quantities of albumin, because they furnish a reaction with mucin—traces of which are said to exist in all urines—I will deal with this question at the outset.

Citric Acid.—When a solution of an acid, such as citric,[1] is run upon or under normal urine of specific gravity 1020 or thereabouts, and kept warm, so as to prevent precipitation of urates, there appears, generally in the course of several minutes, along the plane of contact of the fluids, a delicate whitish zone, which gradually becomes somewhat more and more pronounced. This reaction is said to arise from the presence of a small quantity of mucin held in solution by all urines, acid as well as alkaline, healthy as well as morbid.[2]

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[1] For example, a citric test-paper, dropped into 20 minims of water, provides a solution sufficiently acid, when run upon the urine, to produce the mucin reaction.

[2] If the observer prepare an acid solution of mucin—as by dissolving by aid of heat the purified mucin derived from ox-bile in water containing a vegetable acid, as citric or acetic; or by precipitating the trace of albumin present in clear

It follows that all acid reagents, employed for the detection of albumin in small quantity by the contact method, are open to the fallacy of the mucin reaction.[1]

But this reaction, concentrated by the contact method, becomes inappreciable when diffused throughout the urine: as when a citric test-paper is dropped into 60 minims of transparent urine. Then, as a rule, the keen observer will either fail to detect any alteration at all, or only one of the slightest :[2] but, if the mucin is present in larger quantity than is usually met with, a slight milkiness will appear; and

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diluted saliva by heat and acidulation, and after filtering, or even without filtering, acidifying and reboiling—he will find that citric or any other acid, will not precipitate the albuminoid. Then, it may be asked, if ordinary acid urine contain a trace of mucin in solution, why is it precipitated by an acid? The explanation appears to me to be suggested by my experiments with the bile-salts. See Ch. xii.

[1] Even the slight acidity of picric acid is not an exception to this rule: for, when the solution of this reagent is not allowed to mix beyond a very limited extent with normal urine of specific gravity 1020 or more, there develops a delicate zone, in the course of a few minutes, which may be mistaken for a trace of albumin, as was the case, I fear in all my earlier observations. If this delicate reaction is not due to albumin, what is its cause, if not mucin?

[2] Except when urates are precipitated—a comparatively rare event—or when bile-salts are present in excess, along with albumin. (See pp. 207-9).

this delicate reaction will put the observer on his guard.

The Mercuric Test-Paper.—On, however, using the mercuric test-paper after the acidification, a very delicate haze, if it can be said to amount to such, may be detected, on holding up the urine under examination to the light, by the side of a tube containing the native urine, shaded by the hand or by some dark back-ground. This very diminutive reaction appears in all healthy urines, and is so slight and usual, that the observer, in the ordinary course of testing, will either not recognize it at all, or, if he does, he will disregard it, or estimate it as a 'constant quantity,' and, therefore, of no clinical significance. When, however, mucin is present beyond the normal proportion, the milkiness becomes recognizable, and suggestive of a trace of albumin.

If the observer take a urine, which, according to the ordinary use of heat and acidulation is free from albumin; filter it, to ensure perfect transparency; pour 60 minims of it into two test tubes of the

same diameter, one for the testing, and the other for checking results; note the slight haze induced by the citric and mercuric test-papers, as compared with the transparency of the native urine; and apply heat: he will find, on nearing the boiling point, the urine under examination will become as clear as the untested specimen; but, on cooling, he will observe an opacity, which far exceeds the original haze, and which, on re-heating, vanishes, either entirely, or almost entirely. Such is the mucin reaction with the mercuric *test-paper*.[1]

[1] The reactions of mucin may be readily studied experimentally by impregnating normal urine with saliva — a secretion which contains a large quantity of mucin. The clear saliva and a solution of salt (say 20 grains to the ounce) should be mixed together in equal parts; and one drop of acetic acid, or a citric paper, should be added to a 4 inch column, which should then be thoroughly boiled, when the milkiness produced by a trace of albumin will appear. This highly muciparous solution is now added to albumin-free urine—in such proportion as the observer may wish to charge it with mucin, *e.g.*, 1 to 1 or 1 to 2. In any case the urine will then become more highly muciparous than is likely to be met with in the course of practice. Filtration may be dispensed with—being slow—if observation be checked by some of the untreated fluid, held by the side of that experimented on. A citric and a mercuric test-paper added to 60 minims, produces an opacity, exactly like that induced by a small quantity of albumin; but it differs from it in completely vanishing when heated. The opacity returns as the temperature

If now, however, the observer employs the *test solutions*, he will, in all probability, obtain results which differ from those produced by the test-papers, the reaction being much more pronounced, and, moreover, not clearing at all with heat. Experiment has shown me, that the cause of this disparity is to be found in the varying quantities of the reagents added to the volume of urine submitted to examination; that when they exceed a certain proportion,—that uniformly supplied by the test-papers to 60$\mathfrak{m}$ of urine,—heat can no longer clear up the haziness, the excess of the mercuric salt preventing solution. I, therefore, regard the test-

of the solution falls, and in the cold it greatly exceeds the original amount. Heat will again disperse it as before. The characteristic feature of the reaction is the great increase of the opacity which follows the clearing up by heat; just, in fact, what occurs with normal urine, and also with urine which contains an excess of mucin. No doubt the observer, taking into account the highly muciparous character of the urine, will be surprised by the slightness of the reaction, after dropping in the test-papers; and he will, moreover, find that 10 minims of it, when added to the 60 minim solution prepared from the test-papers (see p. 122), gives the faintest tinge of milkiness, which heat, far short of boiling, completely removes. If now a trace of albumin be communicated to the mucin-charged urine—as by adding a little albuminous urine—the test-papers will produce an opacity, which heat will clear up only to a certain degree; that which remains over being due to the albumin.

papers as possessing a distinct clinical advantage over the solutions.

If the observer charge the normal urine with a trace of albumin, by adding a few drops of an albuminous urine, he will, on using the test-papers, fail to disperse the slight opacity by heat, even when applied to the boiling point. I therefore conclude, that in employing the mercuric *test-paper*, mucin must be classed with urates and all other possible fallacies which are dispersed by heat, and are thus proved to be non-albuminous. And this position, is, moreover, confirmed by all my observations on the working of these test-papers during the past two years; for I have invariably found, that an opacity produced by them, that would not vanish with heat, was *albumin, and nothing but albumin*—a fact proved by the heat test, to which I have been in the habit of appealing for verification.

My clinical experience of this test-paper also leads me to estimate an objection to it on the score of mucin, as of but little practical importance; for, in

any case, it can only apply to such small quantities of albumin as are clinically quite insignificant, and then heat comes in as a corrective.

But, with the view of obviating the rather frequent resort to heat, which, in careful testing, the test-paper used in the manner hitherto followed—*i.e.*, dropped into the urine—is apt to provoke, I have for some time followed a method, which not only affords a negative result in all normal urines, but reduces to an infinitesimal degree the liability to error from mucin and other causes (see p. 122.)

The Ferrocyanic Test-Paper reacts but little with the urinary mucin, and it certainly has not once led me to suspect the presence of albumin, which could not be readily demonstrated by other tests.

The Mercuric Test-Paper.

Potassio-mercuric iodide was brought forward as an albumin precipitant by M. Chas. Tanret, of Paris.[1] According to

[1] See *Journal de Connaissances Médicales*, Mai 15, 1872; also "*Recherche et dosage de l'albumine dans l'urine*," *Bulletin de Thérapeutique*, 15 août 1877, p. 308.

my observations it is the most sentitive test known. The precipitate it produces, being dense, bulky, and white, enables the smallest quantities of albumin to become more apparent than when thrown down by other reagents. The keenness of the test is indeed so great in attacking every vestige of proteid in the urine, that on this very account objections have been raised to it: for it has been alleged, that it induces a reaction in the majority of normal urines, and brings within view traces of albumin of no clinical significance.

In order to meet this objection I no longer advise the test-paper to be dropped into the urine: but to be so used as to furnish three ranges of albumin-detecting power; namely, one on a par with that of nitric acid, one with that of heat, and another of intermediate degree. (See p. 123-4).

Bodies Precipitated.—Used in this way, the only substances thrown out of solution by the test-paper are:—

(1) *Albumin.*

(a) *Native proteids.*—Serum-albumin, and globulin.

(b) *Albuminates.*—Acid and alkaline albumin.

(2) *Peptoid bodies.*

(a) *Peptone.*

(b) *Hemi-albumose.*

(3) *Alkaloids.*

When a precipitate appears, the solution should be boiled. If the opacity remains without change, or is intensified rather than otherwise, it is caused by a form of albumin: if, however, it clears up, either partially or entirely, a peptoid body, or an alkaloid (see below) is present along with albumin or without it; and in this case, as the solution cools the opacity returns and acquires its original intensity.

Alkaloids.—When a patient is taking vegetable alkaloids, such as quinine, morphia, &c., the mercuric test-paper precipitates them like albumin. But if the observer suspects the presence of an alkaloid in the urine, he will determine the matter before testing for albumin, by dropping the reagent paper *only* into the urine, when an opacity will appear if an alkaloid is being eliminated by

the urine ; otherwise the transparency[1] of the urine will remain unimpaired, and the citric test-paper may be added to determine the precipitation of any proteid present. Should the observer detect an alkaloid, he may either select the ferrocyanic test-paper (which does not precipitate alkaloids), or test for albumin, by dropping the mercuric and the acid test-papers into the urine contained in another test tube, and compare the two opacities. Inasmuch as the mercuric precipitate of alkaloids is soluble with heat, any opacity remaining over after boiling the urine, rendered turbid by using the acid along with the reagent paper, is albumin.

The Ferrocyanic Test-Paper.

When employed after the methods to

[1] It is somewhat curious that the mercuric chloride should cause a precipitate in non-acidulated urines, while another mercuric salt—the potassio-mercuric iodide—does not. Some years ago, Dr. John Greene, of Birmingham, used the mercuric chloride (without acidulation) for the purpose of precipitating a body, denominated by him 'leth-albumin,' which is found in all urines in varying quantities. (See *Brit. Med. Jour., vol. ii., 1879*). In a notice of the second edition of this little work, which appeared in the *Birmingham Medical Review*, the potassio-mercuric iodide as a test for albumin was actually called in question because of the reaction of mercuric chloride with 'leth-albumin'!

be described, this test-paper forms a very reliable work-a-day test for albumin.

Bodies precipitated.—The behaviour of the ferrocyanic test-paper on the proteids of the urine differs from that of the mercuric; for, while this precipitates every member of the group without exception, the ferrocyanic exempts the peptones.[1] In this respect it must be classed with nitric acid, which detects every form of proteid except peptones.

In discovering very small quantities of albumin—such as those beyond the range of nitric acid—the ferrocyanic is somewhat less sharp than the mercuric test-paper; for, while the latter reacts instantly, the former does so gradually in the course of the minute to be devoted to the observation. But, when albumin is

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1 The reader will bear in mind, that experiment shows that the ferrocyanic test-paper freely precipitates peptones in mere aqueous solution, but fails to do so when it is dissolved in salt water or in urine. Kühne has recently shown *(Zeit. für Biol.* Brand. xix.*)* that potassium ferrocyanide does not precipitate hemi-albumose, when there is an excess of sodium chloride, or of the reagent: inasmuch, therefore, as the test-paper, or the urine does not provide that excess, the ferrocyanic test does not exempt hemi-albumose as well as peptone from precipitation.

present beyond traces, the ferrocyanic precipitation is as decisive as the mercuric.

In using the ferrocyanic test-paper the observer does not require to be on his guard against a quasi-albuminous precipitate from alkaloids present in the urine. In fact, when this test-paper is employed after the improved method which provides three ranges of albumin-detecting power, there are no fallacies to be encountered. Heat is, therefore, not required as a corrective; and this is fortunate, for, though warmth sufficient to dissipate urates—as when the test-paper is merely dropped into the urine—does not of itself induce an opacity from decomposing the test, boiling does.

The Modes of Testing.

The specimen of urine submitted to examination should, if possible, be clear (see p. 18), and this precaution is essential if it contain organic elements—pus, blood, &c.

The observer may follow one or other

of the following modes of testing: and of the two, I give decided preference to the first.

Method I.

A reagent (mercuric or ferrocyanic) and a citric test-paper are dropped into the test tube: and water[1] is added to the 60m line.

After gentle agitation for half a minute or so, the test-papers are removed, and the transparent solution is ready for the testing.

The pipette, containing the suspected urine, is held in a vertical position over the tube, and the urine is delivered in drops: the number of drops to be added varying with the reagent selected and the range of albumin-detecting power preferred.[2]

[1] It is immaterial whether the water be soft or hard: it is only essential it should be clear.

[2] This matter I carefully determined by experiment. An albuminous urine was diluted by normal urine, until it failed to afford an immediate reaction with nitric acid run down below it: but provided a very delicate zone in the course of a minute. The urine was then regarded as containing a trace of albumin according to nitric acid. How much of it was required to produce a slight but detectable reaction in one minute by the mercuric and ferrocyanic test solutions prepared from the test-papers? Experiment showed that 4 drops were needed by the former, and 6 drops by the latter,

The Nitric Acid Range.— If 4 drops of the urine, added to the mercuric solution prepared from the test-papers or 6 drops to the ferrocyanic[1] solution, do not produce a *trace* of milkiness, when the contents of the tube are viewed against a dark back ground, the observer may safely infer, that if albumin is present, it is in so small a quantity, that nitric acid, applied after the 'contact' method for one minute, will not discover it. If a slight milkiness is apparent, it will represent a trace of albumin detectable by nitric acid. The degree of opacity produced, will of course be increased on dropping in the urine up to the next range of albumin-detecting power: and any doubt as to a reaction on the verge of the nitric acid range will thus be resolved.

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before a delicate milkiness was apparent when the test tube was held before a dark back-ground. Then it was found, that when the urine was diluted by a solution of salt five-fold, heat with acidulation detected a trace of albumin. How much of this further attenuated albuminous urine was needed to produce a slight reaction with the test solutions? 20 drops in the case of the mercuric, and 30 in that of the ferrocyanide.

[1] The observer should give the ferrocyanic solution a minute, in which to develop a reaction from a trace of albumin.

The Intermediate Range. — I propose this for the purpose of detecting a trace of albumin, which cannot be demonstrated by nitric acid in one minute, but can be readily shown to be present by heat and acidulation. For the mercuric test 10 drops, and for the ferrocyanic 15 drops are required.

The Heat Range.—When albumin is present in such small quantity as to be indicated by heat after proper acidulation as a fine haze, experiment has shown, that a corresponding reaction is produced in the mercuric and ferrocyanic solutions, when the urine is added in the proportion of 20 drops to the former, and 30 drops to the latter.

These several ranges, therefore, require the following quantities of urine to be dropped into the test solutions :—

	Mercuric sol.	*Ferrocyanic sol.*
Nitric Acid	*4 drops or 2m* ..	*6 drops or 3m*
Intermediate	*10 ,, 5m* ..	*15 ,, 7m*
Heat	*20 ,, 10m* ..	*30 ,, 15m*

Heat must supplement the Mercuric Test if a reaction appears.— In the case of the mercuric test, if a

reaction occurs, the solution should be boiled, so as to prove the presence or absence of one of the diffusible proteids—peptone, or hemi-albumose. If the opacity is unaffected by heat, or is intensified by it rather than otherwise, it is albuminous; but if it is diminished, or is entirely removed thereby, presumptive evidence is afforded of the presence of a peptoid body, either along with albumin, or alone.[1] The mercuric test supplemented by heat, therefore, provides the observer with a fuller knowledge of the proteids which may appear in the urine than the ferro-cyanic, which precipitates albumin only.

Urines turbid from Urates and Phosphates.—Though, of course, it is always desirable to take a clear sample of urine, I find, in following this mode of testing, the mere presence of lithates and phosphates does not impair the delicacy of observation; for, the turbidity of the drops clears up as they mix with the solution, and the transparency is not impaired by them if the urine is albumin-

[1] According to my observation, this mode of testing presents no other reason than this for the corrective use of heat.

free. Moreover, all other modes of albumin-testing in the cold are liable to confusion from the precipitation of urates —a fallacy to which this is not open.

Reaction with mucin not apparent.—So far, I have not been led to an inaccurate conclusion from the mucin reaction: and it must be apparent, from the small quantity of urine required —especially when the testing proceeds on the nitric acid, or even the intermediate range—that the liability to this source of error must be quite insignificant.

Quantitative Albumin.—This mode of using the test-papers is but the first stage of the method which I follow for approximately determining at the bedside the quantity of albumin: so that, if a reaction appears with the small quantities of urine required merely for the qualitative testing, the observer may proceed at once to the quantitative estimation described in the next chapter.

Method II.

If the density of the urine exceeds

1010, it should be diluted with an equal part of water: or the sample of urine, in which the specific gravity has been determined, should be used without further dilution.

Sixty minims of it are transferred to the test tube.

It is rendered strongly acid by dropping into it a citric paper,[1] which may be allowed to remain, or may be withdrawn, after the interval of a few seconds.

The reagent paper[2] is then let fall into it, and the observer awaits the result, and should not shake the tube with a view to hasten the reaction.

If albumin is present in small quantity —*e.g.*, a tenth of a *per cent.* or less —a whitish cloud will gather about the

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1 If the urine has a distinctly ammoniacal odour, it may, perhaps, be safer to use two citric papers.

2 If the presence of an alkaloid be suspected, the observer should first of all use the mercuric test-paper, and afterwards acidify with the citric; for then a milkiness that appears prior to the acidification, will be caused by an alkaloid, and an opacity, or an increased opacity that follows it, will arise from the proteid present. I prefer, as a rule, to acidify in the first instance, because many urines—those containing earthy phosphates in suspension—are clarified thereby, and any reaction that follows is thus rendered more definite.

paper, and will collect in the lower half of the column of urine: if there be only a trace, the opacity will of course be slight, and will be more readily detected by intercepting the light by a dark background, such as the coat sleeve, &c.; while, in striking contrast, the upper part of the urine will remain clear. If, however, the albumin is met with in larger proportions, it does not usually produce a haze, but coagulates about the paper, and drops down in clots: the observer will then note the gathering of the precipitate in the lower portion of the urine into a cloud, the density of which varies according to the amount of albumin, while the urine above retains its transparency. The contents of the tube may now be shaken up, when the whole of the urine under examination becomes less or more opaque, in proportion to the quantity of albumin present. In the case of the mercuric test, heat should be applied, and any turbidity that remains after boiling is albumin.

If, on the other hand, after dropping in

the reagent paper, the urine preserves its brightness, or any slight turbidity it possessed prior to testing is not increased, the observer may safely infer it is free from albumin.[1]

The Methods originally proposed.—In the former editions of this work I directed the test-papers to be dropped into the urine without dilution. But I no longer advise this mode of observation: because experience has shown that it is open to certain fallacies, which are apt to mislead the observer; such, for example, as the not infrequent precipitation of urates in concentrated urines—a precipitation which often wonderfully resembles the albuminous one—and the mucin reaction. It is true that heat is a corrective—at any rate with the mercuric test-paper—but, having to resort to it frequently, and here and there merely to disprove the presence of albumin, is somewhat troublesome. Then again, cases have been met with in which,

[1] In using the *compound* mercuric test-paper, the observer merely requires to drop one into the diluted urine. The reaction, however, does not appear quite so quickly as when the acid and the reagent test-papers are applied separately.

though the urines were very highly charged with albumin, no precipitate fell when the reagent paper was dropped in; because, the instant it came into contact with the heavy load of albumin, the precipitant became locked up by a dense film of coagulum, which formed all over the paper.

Hence, experience has drifted me to one or other of the modes of testing just described: the first obviating entirely the fallacies to which the original method was liable; and the second minimizing them.

I also suggested the 'contact' method as an effective way of using these test-papers—a solution, prepared from the reagent paper, being run upon the acidified urine: a zone of precipitation appearing along the plane of contact of the fluids, when albumin is present. But as already indicated (see p. 110), this method of albumin testing is liable to the fallacy of the mucin reaction; and a zone of amorphous urates, which will simulate albumin, may also form and mislead the observer.

CHAPTER VII.

ALBUMINURIA: QUANTITATIVE ALBUMIN.

The Methods.—The test-paper mode of urine-testing admits of two methods, by which the quantity of albumin may be determined on the spot, as an addendum to the qualitative observation: namely, one which provides at once the amount of albumin as a fraction of the column of urine—just as the mode of deposition after boiling and acidulation furnishes in twenty-four hours the same information; and the other expresses the quantity as so much *per cent.* The former method has the advantages of putting the quantitative information in the form familiar to all practitioners, and of being sufficiently approximate in the preliminary enquiry at the bedside: while the latter affords

more precise results, and is perhaps better adapted to observation at home.

Method I.

The Quantity of Albumin Expressed as a Fractional Part of the Column of Urine.

The method of deposition, as ordinarily performed after boiling and acidulation, furnishes precipitates which in bulk are not strictly proportionate to the amount of albumin — the smaller quantities of albumin, though of course appearing less bulky than the larger, providing *relatively* less compact and apparently greater deposits. And besides this source of irregularity, there is another frequently overlooked: and that is the time during which the albumin is allowed to settle; for unless it be uniform, not only with one practitioner, but with all, the data thus obtained are not comparable — or they can only be collated in the sense that it is justifiable to reckon fives as nines, or sevens as fours, and the like.

The Mode of Testing.—The quantitative method, which translates at once the amount of albumin as so much bulk of coagulated deposit, is founded on the data provided by the subsidence of twenty-four hours.

The practitioner having determined the presence of albumin by the first described qualitative mode of procedure (see p. 126) will ascertain an approximate notion of the amount by observing the following directions.

He places immediately behind the tube the card on which fine lines are printed (see ch. xiv.): and selects a good reflected light.

So long as the lines are distinctly visible, he adds the albuminous urine according to the stages marked on the tube (see ch. xiv.)—shaking the contents after each addition: and when, from the increased opacity, they pass out of view, the amount of albumin, as so much deposit in twenty-four hours, is read off. In this way the observer obtains a ready gauge of ten different proportions of albumin.

If, after adding a certain quantity of the urine, the lines become more visible than before, it is useless to proceed further: for the urine in that case contains less albumin than is represented by $\frac{1}{8}$ deposit.

When the lines are occluded by the mere addition of urine to the lowest mark on the scale, the urine contains so much albumin as to solidify on boiling.

Method II.

The Percentage Estimation of Albumin.

The apparatus required are:—

(*a*) A permanent standard of opacity representing $\frac{1}{10}$ *per cent.* of albumin precipitated by the mercuric or the ferrocyanic test-paper. (See ch. xiv).

(*b*) A flattened tube of definite diameters, and graduated. (See ch. xiv).

(*c*) Printed lines. (See ch. xiv).

The Mode of Testing.—If the qualitative observation has shown the presence of albumin in pretty considerable quan-

tity, a measured portion of the urine should be diluted to twice, or three, or four times its bulk: and the results of the quantitative testing must then of course be multiplied by the number of dilutions. But if the urine has been found to be only moderately albuminous, it is not advisable to dilute it.

Fifty minims of the urine—or of the diluted urine—are poured into the flattened tube: the observer being careful to make the lowest part of the meniscus on a level with the graduation line.

A reagent paper (mercuric or ferrocyanic) along with the citric paper is dropped in, and the contents of the tube are shaken, or are made to oscillate up and down the tube while the thumb is held over the mouth for about a minute, when all the albumin will be precipitated.

The card bearing the printed lines is placed close behind the tube and the standard of opacity, and if the opalescence of the precipitated albumin is seen to exceed that of the standard, water must be added until the two are exactly

equalized ; and dilution may proceed pretty freely if the lines are completely obscured, but with some care,—not more than 10m at a time,—when it is obvious the opacity only somewhat exceeds that of the standard, or the limit thus provided is being approached. The observer may remove the test-papers shortly after he begins to dilute the urine, otherwise they may obstruct observation.

After each addition of the water, uniformity of the opacity is secured, by placing the thumb over the mouth of the tube, and gently mixing up the contents ; then is the time to view the printed lines, before the uniform opalesence after agitation gradually breaks up into flocculi.—as it does in a minute or so.

In making an observation it is advisable to distinctly overstep the limit furnished by the standard opacity, and then to subtract 10m for this excess.

If on diluting to 200m (the limit of the scale provided by the test tube) the opalescence still over-blurrs the printed lines, 100m should be removed, and

dilution should proceed until the opacity is reduced to that of the standard. In this case, in calculating the amount of albumin, the dilutions acquire a double value to that which obtains on the first filling of the tube.

The percentage of albumin is calculated by multiplying ·1—the determined value of the standard opacity—by the number of times the volume (50m) of the urine has been increased by dilution; *e.g.*, when it is needful to dilute the 50m of urine to 200m the amount of albumin is ·4 (·1×4=·4). Inasmuch as the proceeding generally finishes off somewhere between equal volumes of the 50m of the urine submitted to examination, it is desirable to know—in order to simplify calculation—what is the value of every 10m of the column reached by dilution: it is ·02 *per cent.*; so that, for example, if it is necessary to dilute the urine to 130m, the observer merely requires to multiply ·02 by 13, in order to express the per centage amount of albumin (·02×13=·26 *p.c.*) I will now take an example, in which it is

advisable—because of the large quantity of albumin present—to dilute the urine twice before the estimation is attempted; and, on determining the amount of albumin present in the diluted urine, it is needful to carry forward the additions of water into the second filling of the graduations—the reading being indicated at 160m. In this case, the first filling of the tube to the 200m represents ·4 (·02 × 20 = ·4), and the further dilution of 60m, after the clearing out of 100m, gives in addition ·24 (·02 × 6 = ·12 × 2 = ·24); therefore, together ·64 (·4 + ·24): but, inasmuch as the urine was increased from one volume to three by water before it was submitted to the estimation, the product must be multiplied by 3, in order to express the percentage amount of albumin (·64 × 3 = 1·92 *per cent.*)

When the opacity is below that of the standard, there is, of course, less than $\frac{1}{10}$ *per cent.* of albumin present. In this case the quantity may still be estimated: for, on viewing the printed lines through the long diameter of the tube, the blurring

equivalent to that of the standard, represents $\frac{1}{20}$ (or ·05) *per cent.* When used in this way, the observer may determine either the presence of this small percentage of albumin; or a proportion still less; or one that stands between ·05 and ·1 *per cent.*

The Quantitative Value of each Test-Paper.—On submitting 50m of urine to examination, the quantitative range of each mercuric test-paper is 1 *per cent.*: and that of the ferrocyanic 2 *per cent.* Inasmuch as these really large proportions of albumin are only met with quite exceptionally, one test-paper will, therefore, cover all the ordinary amounts: and certainly the heavier quantities in all instances, if the observer in such cases dilutes the urines before estimating them.

The Quantity of Albumin met with.—As a rule albuminous urines contain less than 1 *p.c.*; only now and then the amount rises to 2 *p.c.*; and it is but a rare observation to find more than from $2\frac{1}{2}$ to 3 or 4 *p.c.* The proportion in blood-serum is only about 5 *p.c.*: and when the

urine contains this large amount, boiling completely solidifies it. The general impression as to albumin appearing in the urine in larger quantities than these is groundless.

The Daily Amount of Albumin discharged. — As with other quantitative estimations of urinary constituents, so with this, it is the determination of the *per cent.* in a portion of the urine of the whole day, and the total amount thrown out during twenty-four hours, that is clinically of most importance. When the urine examined is part of the daily yield, and the latter has been measured, it is not difficult to arrive at the total daily loss of albumin in intelligible figures : for, it is only necessary to multiply the *per cent.* by $4\frac{1}{2}$[1] to arrive roughly at the number of grains to the fluid ounce ; *e.g.*, albumin ·6 *p.c.*, the 24 hours' urine 40 oz., $(\cdot 6 \times 4\frac{1}{2} \times 40) = 108$ grains daily discharge of albumin.

[1] The correct figure is 4·36.

CHAPTER VIII.

ALBUMINURIA: THE CLINICAL SIGNIFICANCE OF ALBUMIN.

A mere sketch possible. — In the limited space at my disposal I can but provide a few memoranda of this large and important subject: which may perhaps enable the reader to revive his clinical experience.

The conditions of each case to be weighed. — Wherever albumin is detected in the urine, the clinical significance of it must be viewed from the individual standpoint: and the conditions that determine it require, of course, to be duly weighed before it can be estimated. It is but a 'symptom' which may indicate a condition of little clinical moment, or may signify serious organic disease. In all cases the important question—*is it due*

to renal disease or not?—will present itself to the observer for solution.

I. *The Albuminuria is intermittent.*

The fact of intermission is of clinical significance.—It is of importance to determine whether or not the albumin now and then disappears from the urine. I do not, of course, refer to the remission of the amount, frequently observed in the urine voided by albuminuric patients in the night or before breakfast; but to the total clearing away of the albumin for varying intervals. When the albuminuria is distinctly intermittent, it is probably not due to chronic disease of the kidneys; it is true that albumin in Bright's disease will sometimes diminish almost to the verge of disappearing—but it rarely vanishes entirely, unless the renal disease recovers.[1]

Functional Albuminuria. — Temporary albuminuria may appear in apparently healthy subjects. The cause is

[1] In cirrhosis of the kidney it is said, however, that albumin is often absent for days; and especially in the early part of the disease.

often slight and obscure, such as dyspepsia and biliousness;[1] or a diet unsuitable, or too rich in proteids;[2] or excessive muscular exertion; or prolonged exposure to cold bathing, or other cause of chilling. The *albuminuria of adolescents* is the best example of this class of cases: in this condition there is often loss of tone, anæmia, or digestive disorder, but not uncommonly the health is good; and the morning's urine before breakfast is generally normal, while that passed after meals and exercise contains albumin—the urine throughout retaining the normal density and colour.

Perhaps the most marked examples of copious temporary albuminuria are witnessed in *bronchocele and exophthalmos*, as first pointed out by the late Dr. Warburton Begbie,[3] who delineated the following

[1] On p. 206 I point out that different degrees of acidity of the chyme &c., may lead to temporary albuminuria and peptonuria, and in ch. xiii. that the discharge of an excess of bile-salt in the urine leads to albuminuria.

[2] There is the well-known instance of the elimination of egg-albumin by the kidneys of certain persons.

[3] *The works of the late J. Warburton Begbie, M.D., &c.*, edited by Dyce Duckworth, M.D., &c. The New Sydenham Society.

urinary features of the ailment: the urine normal in colour, density, and in other respects; but containing albumin in considerable or large amount after meals (the quantity being much greater after breakfast than after luncheon, dinner, or evening meal) but absent during the hours of fasting—as before meals and after sleep. But in all forms of intermittent albuminuria the urine is more albuminous after breakfast than after the other meals,[1]

Temporary albuminuria may also be induced by:—

(1) *Medicinal irritants*, such as cantharides, turpentine, carbolic acid, &c.

(2) *Alcoholic excess.*

(3) *Menstruation.* "In a good many women, for a few days before and for a few days after menstruation, the urine free from blood-discs, leucocytes, or pus, contains, sometimes continuously, sometimes intermittently, small quantities of albumen."[2]

[1] When albuminuria is *persistent* the urine contains a larger proportion of albumin after breakfast than at other times: and the percentage, as well as the absolute amount, is least during the night.

[2] *Albuminuria* by Sir Andrew Clark, Bart., M.D., *Brit. Med. Journal*, 1884, vol. ii., p. 312.

(4) *Febrile movement*—zymotic or inflammatory (see p. 154).

(5) *Hæmoglobinuria.*

(6) *Neurotic disturbances* (see p. 155). "Among twenty men entering a competitive examination, lasting a week, three are found to have albumen in the urine."[1]

(7) *Strangulated hernia.* Of 74 cases, observed by Dr. Englisch, 39 had albumin in the urine, which either appeared simultaneously with the strangulation, or several days later; and vanished in from 24 hours to 4 days after taxis, or successful herniotomy. According to Dr. Englisch's observations, albuminuria—when not pre-existent—indicates involvement of the intestine in the strangulation : for when absent, only omentum or an appendix epiploica was found in the hernial sac.[2]

(8) *Heart disease*, &c. (See p. 153).

(9) *Bile-salts* eliminated by the kidneys.

(10) *Acute nephritis.* (See p. 152).

When the observer suspects temporary albuminuria he should examine specimens

[1] Sir Andrew Clark, *op. cit.*

[2] See *Brit. Med. Journal*, 1884, vol. ii., p. 672.

of the urine voided two hours after a meal (such as breakfast) and after exercise. In all cases the density keeps up, and the colour does not diminish.

II. *The albuminuria is persistent.*

The cause is Urinary.—When the albuminuria is permanent, the cause is nearly always referrible to the urinary organs—and to the kidneys in particular.

If the amount be small—*e.g.* a mere trace—and the urine is hazy when voided, it may be merely pus-derived: as when there exists an inflammatory condition of some part of the urinary tract, or a purulent discharge; the urine of women, and that of elderly men is very frequently of this character.

The cause is Renal.—The permanent presence of a large quantity of albumin is almost invariably due to chronic renal disease[1], and, as a rule, the probability of the renal origin is in pro-

[1] Several instructive exceptions have been published: but they are only exceptions, and do not invalidate this general proposition.

portion to the amount. It is true, that very often the urine of chronic Bright's disease—especially in the cirrhotic kidney — contains but a small percentage of albumin: but, inasmuch as in such cases, the quantity of the twenty-four hours' urine is excessive—often four or five pints —the aggregate amount of albumin discharged is really large.

If the freshly voided urine containing albumin—in however small amount—is pale, and watery, the observer will suspect the kidneys: for such is the urine of a large number of cases of chronic Bright's disease—especially of the cirrhotic form. In many cases (as in cirrhosis) the watery looking urine is transparent: but in others it is not quite clear.

The observer will bear in mind, that the ordinary characters of the urine in chronic renal disease are apt to be modified by complications — such as phthisis, heart disease, inter-current attacks of pyrexia, and liver derangement —the secretion becoming high-coloured, and depositing lithates.

The non-renal origin of albuminuria, even when persistent, is supported by the urine—especially that of the twenty-four hours—retaining its colour and specific gravity.

III. *The quantity of albumin.*

Besides estimating the percentage, or the deposit-proportion, the observer should calculate the total daily amount of albumin discharged from a sample of the twenty-four hours' urine. (See p. 140).

The quantity is very small: minimal albuminuria.—The clinical significance of mere traces varies with the circumstances of each case. It may be trifling, as when the urine contains pus cells, blood corpuscles, or spermatic elements: but in such cases it is important to detect pyelitis—apt to exist in a mild form without local discomfort—which may be the starting point of chronic renal disease, from the inflammation insidiously spreading upwards into the kidneys. But all cases in which traces of albumin are detected in the urine perfectly transparent

when voided, require sifting with more than ordinary care: for, there may be commencing renal disease, or the kidneys may be undergoing cirrhotic degeneration; or it may turn out that such minimal albuminuria is merely 'functional' (see p. 142). Whenever albumin is found in small quantity, and some doubt exists as to its origin, the observer should always secure a sample of the urine passed about two hours after breakfast—as this always contains the maximum proportion of albumin. In investigating doubtful cases of albuminuria it is of great practical importance to avoid alarming the patient unnecessarily—as the neurotic disturbance thus induced may operate injuriously on the kidneys (see p. 145). Happily it is now well known, that the detection of albumin does not of necessity imply the existence of progressive disease of a fatal character.

The quantity of albumin in the different forms of renal disease.—In *acute nephritis* after scarlatina the amount of albumin is always large: and

the urine frequently—at the height of the disease—solidifies on boiling. The percentage, as a rule, varies from ·8 to 2·5: and as much as from 100 to 400 grains may be discharged in twenty-four hours.

In *chronic renal disease* the quantity of albumin varies with the form it assumes, and the stage it has reached. In *chronic nephritis* (smooth white kidney) albumin is discharged usually in large quantity: *e.g.* from ·6 to 2·0 *per cent.*, or from $\frac{1}{3}$ to $\frac{2}{3}$ deposit in 24 hours; and the total daily amount may reach 300 grains. In the *cirrhotic kidney* the quantity of albumin is small: and in the early stage it is said to be absent. Often the amount does not exceed ·1 *per cent.* or $\frac{1}{12}$ deposit: but inasmuch as the discharge of urine is generally excessive, the daily quantity of albumin eliminated is greater than the percentage suggests; it generally varies from 50 to 150 grains. In the *waxy kidney* albumin is, in the early stage of the disease, discharged in small proportion in a large quantity of urine: but, as the disease progresses, the percentage as well as the

absolute amount of albumin increases considerably, while the urine diminishes. The proportion of albumin will often rise from ·3 *per cent.* to 1·5 *per cent.*: and I have noted a rise in the daily amount from 90 to 250 grains.

In *functional albuminuria* (digestive, neurotic) the amount of albumin is generally small—often only from $\frac{1}{20}$ to $\frac{1}{10}$ *p.c.* or even less—but in several recorded cases, in which evidences of renal disease were absent, and the patients recovered, it was moderately large. In goitre the quantity is often considerable.

IV. *An Epitome of the causes of Albuminuria.*

The causes are often compound.—In any particular case of albuminuria several pathogenic conditions may co-exist. For example, a gouty man commits an indiscretion in diet, or is chilled, or is excited, or is unusually worried: when albumin either appears in the urine, or, if pre-existent, increases; and, as the temporary disturbance ceases, either vanishes or diminishes.

The following table summarizes the principal causes of albuminuria.

I. THE PRIMARY CAUSE OF THE ALBUMINURIA IS SOME MORBID CONDITION OF THE KIDNEYS OR OTHER PART OF THE URINARY APPARATUS.

(*A*) *The cause is renal.*

Injury: severe contusion of the loins.

Concretionary Irritation: a calculus, or diminutive concretions lodged in the tubuli uriniferi.

Active congestion from

(*a*) *A chill: e.g.*, prolonged cold bathing.

(*b*) *A medicinal irritant: e.g.*, cantharides, turpentine, carbolic acid, salicylic acid, nitrate of potash, cubebs, copaiba, &c.

Acute nephritis from

(*a*) *Cold.*

(*b*) *Alcoholic excess.*

(*c*) *Following scarlatina*, or other febrile or zymotic ailment.

Chronic Bright's Disease,

(*B*) *The cause is referrible to some part of the genito-urinary mucous tract.*

Pus or Blood mingling with the urine from pyelitis, cystitis, morbid growth (*e.g.* villous tumour), menstrual flow, &c.

Muco-Purulent Discharge from vagina.

Albumino-Mucous Discharge or Secretion from the prostatic area (spermatic fluid, &c.)

II. THE ALBUMINURIA IS SYMPTOMATIC OF SOME CAUSE AFFECTING THE KIDNEYS, BUT OUTSIDE THE URINARY APPARATUS.

Passive Congestion of the Kidneys from increased tension in the renal vein, as in

(*a*) *Disease of the heart.*

(*b*) *Emphysema* with bronchitis.

(*c*) *Pleuritic effusion.*

(*d*) *Gravid uterus or other abdominal tumour* (ovarian, aneurismal, &c.)

(*e*) *Cirrhotic liver.*

Fever.

(*a*) *Zymotic:* as in scarlet fever, diphtheria, measles, small-pox, typhus, erysipelas, cholera, yellow fever, ague, pyæmia, rheumatic fever, &c.

(*b*) *Inflammatory:* as in pneumonia, peritonitis, acute articular rheumatism, &c.

Hæmolytic and other defects of the Blood and Tissues.

(*a*) *The corpuscles undergo solution*—hæmoglobinuria.

(*b*) *Hydræmic states*–purpura, scurvy, chlorosis.

(*c*) *Uricæmia*—gout.

(*d*) *Poisoning*—lead, phosphorus, arsenic, mercury, iodine, morphia, alcohol.

(*e*) *Chyluria*, *lymphuria*, (see p. 34).

(*f*) *Syphilis.*

(*g*) *Tuberculosis.*

Digestive Disorders.— Food-albuminuria. Hepatic albuminuria.

(*a*) *Food in excess. Salt in diminished quantity.*

(*b*) *Dyspepsia, &c.*

(*c*) *Hepatic disorders:* albuminuria induced by the elimination of bile-derivatives by the urine, (see ch. viii.)

(*d*) *Oxaluria*: as in young men from eighteen to thirty.[1]

Neurotic Disturbances.

(*a*) *Mental worry and over-strain.*

(*b*) *Vascular bronchocele and exophthalmos.*

(*c*) *After epileptic seizures.*

(*d*) *Delirium tremens.*

(*e*) *Tetanus.*

(*f*) *Cerebral hæmorrhage and concussion.*

Cutaneous Irritation: chemical, thermic, &c.,

Strangulated Hernia.

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[1] Sir Andrew Clark *op. cit.*

CHAPTER IX.

GLYCOSURIA: THE DETECTION OF GLUCOSE BY TEST-PAPERS.

An Alkali necessary.—All the reagents employed as tests for sugar are either caustic alkalis, or bodies which must be associated with an alkali; but in the latter case it is by no means necessary to use a caustic alkali. I have, for example, proved by experiment, that carbonate of soda will work quite satisfactorily with mercuric cyanide, picric acid, indigo-carmine[1] and tartrate of cuprammonium. I have used all these tests in the form of test-paper with good and reliable results: but the carmine and cupric have appeared to me, not only the best adapted to this mode of observation, but the least open to fallacies. (See pp. 167—176).

[1] In the case of the indigo-carmine test carbonate of soda *must* be used instead of a caustic alkali, which discharges the blue colour even in the absence of a reducing agent, such as glucose. (See p. 171).

I. The Indigo-carmine Test-paper.

The Indigo-carmine test-solution valueless for clinical purposes.—When a solution of indigo-carmine (the sulph-indigotate of sodium), alkalinized by carbonate of soda, is boiled, and is then kept heated, the rich blue colour remains without change; but, when a drop of a solution of glucose or of saccharine urine is let fall into the hot solution, there instantly strikes up a series of beautiful colour changes which culminate in pale yellow. Unfortunately for clinical use the indigo-carmine test in an aqueous form is valueless; because, when the carmine and the carbonate of soda are present in the same solution, the test undergoes a gradual change which renders it useless—the rich indigo-blue slowly giving place to a faded pale green; and, when kept apart as two solutions, they must be used on every occasion in exactly the same proportions, otherwise the results obtained are not comparable, and the observer fails to gain a notion of the approximate amount of glucose

present—that useful information, in fact, which every good test for clinical purposes should provide. Hence, the liquid preparation of the test is valueless as a clinical instrument; and the grave defects which belong to it must have speedily led to the disuse of it by those who followed in the wake of Mulder, who introduced it.

The Indigo-Carmine Test-Paper, however, not only meets these disadvantages, but amplifies the powers of the test.

(*a*) Each paper is charged with the same definite quantity of the reagents; it thus provides a uniformity for the qualitative testing, which also becomes a standard of known value for the quantitative estimation. An additional range of sensitiveness is, moreover, provided by the paper containing a uniform charge of carbonate of soda, when used with the ordinary test paper.[1]

(*b*) The test-paper furnishes with soft

[1] I prefer the paper in the 'compound' form—the constituents being kept apart in separate papers united by a layer of rubber, which, when heated in water, separates, and rolls up to the surface out of the way.

or distilled water a perfectly transparent alkaline solution of the carmine—which is, moreover, of a rich blue colour that undergoes no change on boiling. On the other hand, a transparent solution of the indigo-carmine is precipitated by carbonate of soda: and though boiling clears up the precipitate, the solution acquires a green tint, which is incorrectly described by Mulder, Méhu, Neubauer, and Vogel as the first stage of the reaction of the carmine with glucose. Unlike the solution, the test-paper, therefore, provides a clean start for the testing: so that the urine to be examined may, with some saving of time, be added before heat is applied, and the first change of colour, which after ebullition gradually appears, can be safely taken as the earliest step in the reaction.

(*c*) The stability of the test-paper is beyond question. The constituents being dry, remain unchanged; and, when dissolved out of the paper, they furnish a freshly prepared solution at each observation.

The Reaction. — The characteristic reaction, which indicates the presence of glucose in the urine, arises almost immediately after a drop of saccharine urine is let fall into the hot solution of the reagent, prepared from the test-paper. A beautiful violet tint suddenly spreads throughout the bright blue solution; very quickly the violet deepens and passes into purple; this in its turn melts into reddish-purple, which gives place to various tints of red, and these as quickly merge into orange-red and orange, and finally the solution becomes of a straw colour, which remains without further change, though the heating is continued ever so long. At this point the paper assumes the same light yellow colour as the liquid. The complete range of this striking colour reaction embraces all the prismatic colours except green, and the order of the appearance of the successive hues is always the same. The reaction is one of great beauty; for the primary colours are not merely pure and sharply defined, but all the transitional and inter-

mixed tints pass quickly before the eye in such richness as one rarely sees in nature herself. Now, on shaking the tube the colours return in the inverse order to that in which they appeared. This remarkable thing is not due to cooling, but to admitting the oxygen of the air into the liquid; for the various hues at any stage of the reaction may be caught and retained for days, merely by corking the tubes full of the solution, and the return of the colours, when the test tube is at rest, always appears first at the surface, and slowly spreads downwards—so slowly that after putting the solution aside for some hours, at least the lower half will still retain its acquired colour.[1]

[1] Inasmuch as the return of the colours is clearly due to oxidation, it will probably be safe to presume that the reaction of glucose on indigo-blue is a process of deoxidation. The first stage of the reaction is pretty clearly the conversion of the blue (indigotin) into the red (indigorubin) isomeric form of indigo—hence the shades of violet, purple and red; and just that small amount of glucose can be added as to secure only these steps of the reaction. The second stage is the gradual merging of red into pale yellow—the colour of indigo-white when dissolved in aqueous alkalis. The whole reaction is, therefore, due to the deoxidizing power of glucose over indigo-blue in the presence of the alkaline carbonate: the blue indigo being converted in the first place into indigo-red, and then into indigo-white.

Experiment has shown that the tint reached in any particular observation depends on the quantity of glucose added to the test liquid: *e.g.*, the reaction may stop at violet, purple, red, &c., and when it thus halts, it can easily be made to proceed to the final stage by adding more of the glucose-charged urine—an additional carbonate of soda paper being added, and the liquid the while being kept hot. This suggests a principle on which to found a mode of quantitative observation. That which I employ is a very simple one; it is based on the complete removal of all the colours below the pale yellow: and on the scale of colours when the quantity of sugar is small (*e.g.*, below 5 grains to the ounce).

Carbonate of Soda Papers.—Test-papers charged with a saturated solution of carbonate of soda are provided for the following special purposes:—

(1) *When hard water is used.* On heating the carmine test-paper in hard water a clear solution cannot be obtained: for the earthy carbonates are precipitated by the alkali. Inasmuch as in this reaction

a portion of the carbonate of soda becomes inoperative — passing into the bi-carbonate — it is advisable to fortify the alkaline charge of the carmine test-paper by using a soda paper as well. When the water is hard it is best to boil the alkaline paper in a measured portion of it before adding the carmine test-paper.

(2) *Excessive acidity of the urine.* The reader will bear in mind that the acids of the urine rob the carmine paper of so much alkali: so that the addition of more than a certain number of drops of urine—varying of course with the degrees of acidity—will at first retard and then prevent the reaction.[1] Invariably submitting only one drop of saccharine urine to the test-paper, and keeping up the heating for not less than two minutes, I have hitherto always witnessed the characteristic display of colours without requiring to use a carbonate of soda paper: so that I

[1] The reaction of solutions of glucose with the carmine paper alone can be stopped by adding certain quantities of urine of average acidity, *e.g.*, that provided by 40grs. to the oz. by about 40 drops of urine; 20grs. by 20 to 25 drops; 5grs. by 7 drops, &c.: but the reducing power of the glucose is again restored on adding a carbonate of soda paper.

am led by observation, to regard the carmine paper as complete in itself for the detection of glycosuria—providing of course the observer uses merely one drop of the urine delivered from the pipette held vertically (see p. 165—note). But it may be well for the reader to bear in mind, that a very exceptionally acid saccharine urine may perchance be met with, which may require also the soda paper. I purposely avoided charging the carmine paper with more soda than it now possesses, because experiment showed me, that it then became too sensitive for a good practical test—one drop of normal urine or of a solution of glucose (gr.$\frac{1}{2}$ to the ounce) for example, then developing a distinct violet in the course of heating for two minutes.

The mode of Testing.—(1) One of the papers should be dropped into the half-inch test tube, and then water should be poured in to the 60$\mathfrak{m}$ mark.

(2) Heat is applied (see p. 108), the tube being gently shaken, and boiling kept up for a second or two. The solution will then be quite blue; and, if the water

added was soft or distilled, it will be perfectly transparent. Any turbidity observed will arise from the use of hard water: in which case a carbonate of soda paper should be dropped into the solution (see p. 162). The test-paper may now be removed, or it may be allowed to remain.

(3) Not more than one drop[1] of the suspected urine is let fall into the tube from the pipette, held in an upright position.

(4) The contents of the tube are again freely boiled for a few seconds: then the tube should be raised an inch or two above the flame, and held without shaking, while the solution is kept quite hot, but without ebullition, for exactly one minute by the watch. If glucose be present in abnormal amount, the soft rich blue will be seen first of all to darken into violet: then, according to the quantity of sugar, there will appear in succession, purple, red, reddish yellow, and finally

[1] The pipette when held vertically will deliver drops of nearly equal size, *i.e.*, about half a minim. But, if the drop is allowed to fall from it in a slanting position, it will be larger, and more liable to variation in size.

straw yellow. When the last named colour has been developed, the observer will find the slightest shaking of the tube will cause red streaks to fall from the surface, and to mingle with the pale yellowness of the solution; and further agitation will, of course, cause the return of purple and violet, and the restoration of the original blue.

The time required for the commencement of the reaction after the boiling of the test liquid, varies in inverse proportion to the amount of glucose present: when the latter is large—*e.g.*, over 20 grains to the ounce—it will extend only to a few seconds; but when small—*e.g.*, from 2 or 3 grains to the ounce—from thirty to sixty seconds may elapse.

If the urine does not contain more than the normal amount of sugar—*i.e.*, under half a grain to the ounce—the colour of the solution at the end of the heating for one minute, will be unchanged.

Care should be taken during the observation not to shake the tube, or to keep up free ebullition. There is besides

another precaution against which the observer, who has no practical experience of this test, should be warned: while keeping the contents of the tube hot, he should not hold the latter up between his eyes and the sky—for then the *early* colour changes may escape observation; but he should keep it below the eye-level, and view its contents by the reflected light of some bright object, such as a sheet of white paper propped up an inch or two beyond the tube, as a back-ground.

The test is as available by artificial as it is by daylight.

Confirmation of results by Fehling's solution.—In applying the test-paper to different urines, I took Fehling's solution as my guide, because it is the best known glucose test.

The results of the working of the two side by side were briefly as follows:—

(*a*) On always submitting one drop of urine to the indigo test, and the presence of sugar being shown, confirmation was invariably provided by Fehling used in the ordinary way.

(*b*) On the other hand, whenever one drop of urine gave no reaction with the test, Fehling's solution did not give the cuprous precipitate.

Experimental Testings with the Indigo-Carmine Test-Paper and with Fehling's Solution compared.—In the last edition of this work I gave in detail a large number of experimental observations on the reduction of these glucose tests by various agents—certain urinary constituents, and medicinal substances which may appear in the urine. At that time the somewhat uncertain clinical position of the indigo-carmine test-paper required such a critical examination : but now, inasmuch as that uncertainty is being removed by experience of the test, and the practical value of it is being realized, there no longer remains a sufficient need for the same scrutiny in elementary data. I will, therefore, merely give an epitome of my observations relating to these matters.

(*a*) *The urinary constituents.*—None of the ordinary constituents of the urine affect the carmine test, but all the free acids of

the urine—uric, oxalic, lactic, &c.,—reduce Fehling's solution.

Of the substances apt to appear in the urine in disease, albumin, peptone, pus, mucus, blood[1], bile, leucin and tyrosin do not react with either test; but dextrin and milk sugar as well as glucose reduce both.

The carbohydrate, inosit, which has been detected in small quantity in the urine of some cases of diabetes and albuminuria, reacts with the carmine, and turns Fehling's solution green—a green precipitate falling, leaving the supernatant liquid blue, but becoming green on reheating. Hence, Dr. Ralfe points out that the indigo-carmine test "may be thus made available for distinguishing between those forms of sugar sometimes present in urine which give no reaction with copper, and which do not readily ferment, and so help to distinguish those cases from true glycosuria."[2]

It has been suggested to me that *stale urine*—which is the favourite reducing

[1] The sugar contained in these fluids may reduce the tests.

[2] *Clinical Chemistry*, p. 155.

agent of some wool-dyers—may afford the reaction; one of the advantages, however, of this mode of testing is the avoidance of decomposing urines, with which no test for glucose can be trusted. I have, however, observed that the test-paper does not produce a reaction with one drop of ammoniacal urine, or of decomposing albuminous urine; and ammonium sulphide in weak solution (but sufficient to reduce Fehling) used in the same way is equally negative, but, when more concentrated, it will reduce the carmine. When ammonia is freely added to diabetic urine, the reaction is not retarded or prevented; and ammonia of itself cannot produce it. But still I would suggest some caution in inferring the presence of sugar in putrifying urine from the reaction with the carmine test-paper, or with any test for glucose.

(*b*) Of *medicinal agents* likely to find their way into the urine, the only ones which react with the carmine are iron sulphate,[1]

[1] "Salts of iron, especially augment very largely the iron of the urine, though the amount passing off in this way is not

and gallic and tannic acids—substances which likewise reduce Fehling's solution.

Clinical and experimental results provided by the Carmine and by the Picrate of Potash Tests.—In all my observations on these elementary data, as well as in my clinical experience during the past two years, whenever the indigo-carmine test-paper afforded a reaction, a corresponding one was obtained by the picrate of potash solution. The picric, as well as the carmine test, reacts with all other forms of carbo-hydrates besides glucose, that may appear in the urine—such as dextrin, lactose, maltose, and inosit.

There is one substance which—though not a constituent of the urine—will discharge the blue colour of the carmine: and that is a caustic alkali—*Liq. Potassæ vel Sodæ.* I think it well to mention this,

known." *The Composition of the Urine, &c.*, by Ed. A. Parkes, M.D., Lond., 1860, p. 142. I have found the urine of patients taking iron freely is apt to give reactions with the cupric, and carmine tests, suggestive of small quantities of sugar over the normal amount. In this connection the observation of Graevecke, that iron in the urine is always in the ferrous condition, is instructive.—*(Archiv. f. Exp. Pharm., vol. xvii., p. 466).*

lest the observer, using a test tube containing a trace of Fehling's or the alkaline picric solution, obtain a reaction with a drop of non-saccharine urine. The caustic alkali converts the blue carmine into a green solution; and on heating all colour gradually vanishes. This reaction is, furthermore, unlike the characteristic one afforded by glucose, in that any remaining colour after heating slowly fades away on shaking the contents of the tube; and, when the solution has become quite colourless, no amount of agitation will restore the colours.

Some Clinical advantages of the Indigo-Carmine Test-Paper.—The high position of Fehling's solution as a test for glucose in urine cannot be questioned; but for two disadvantages which belong to it—the liability to change on exposure to light and air, and the caustic properties which condemn it for bedside or out of door work—no one would desire a substitute. It has undoubtedly yet much sound work to do, and I have no wish to disparage it. Still,

like every other urinary test, it is not equally good all round. Where it is weak and apt to fail, the indigo-carmine test, as here presented, appears to me to supply useful supplemental aid—apart from other clinical advantages.

(1) Sugar in small quantity along with much albumin, may be overlooked by Fehling. The search for sugar by this test in albuminous, bloody, or purulent urine, should be preceded by the precipitation of the albumin, and by filtration. These procedures are, however, unnecessary when the indigo-carmine test-paper is used; for, it has been proved by repeated observation, that it will detect sugar—in any proportion, and as readily as in ordinary diabetic urine—in the presence of albumin, peptones, blood, pus, &c.

(2) It is well known that uric acid will reduce Fehling's solution: but this body does not react with the carmine test. The latter is unaffected by urates: the former is, however, apt to give with them a cuprous precipitate, which may easily

lead to a false inference. On this point Prof. Cameron, of Dublin, gives the following very useful caution in applying the cupric test. "I occasionally find urine with a very high specific gravity, and with a, so to speak, diabetic appearance, to be quite free from sugar. On several occasions, in specimens of urine believed to contain sugar, I could not detect a trace of that substance. A few months ago I examined the urine of a man who had been treated for diabetes. The urine had a specific gravity of 1035, and, on being boiled with Fehling's solution, it gave a copious precipitate of cuprous oxide. There was something in the appearance of the precipitate, and in the slow way in which it made its appearance, that led me to suspect that it was not produced by sugar. This proved to be the case, for on treating the urine with yeast no carbonic acid (save a mere trace) was evolved. The presence of large quantities of urates in urine causes a brown precipitate with Fehling's solution. The urates, even when abundant, do not

always separate as the characteristic 'brick-dust.' I have found very large quantities of urates of ammonium in urine which remained clear on standing, but which gave a brown precipitate on being boiled with Fehling's solution." (*Dublin Journal of Medical Sciences*, April, 1883). In such cases the clinical value of an appeal to the carmine test must be apparent; for it will in a ready and simple way obviate the fallacy which makes the cupric test untrustworthy.

(3) Dr. Ralfe has suggested (see p. 169) that it may prove a valuable supplement to the other tests for sugar, by virtue of its power to detect the saccharoid bodies which may appear in the urine that do not react with copper, or that do not readily ferment. The reader will, however, bear in mind that hitherto observation has shown that such bodies—*e.g.*, dextrin, lactose, inosit,—but rarely appear in the urine; and that, therefore, when the reaction is obtained with the carmine the presence of glucose may be pretty safely inferred.

(4) The capacity of the carmine test-paper to afford information as to the approximate quantity of sugar in the course of the search for this body (see Chapter x.) is a valuable working property; for it enables the practitioner at once to form an estimate of the cases of glycosuria examined for the first time, and of the effects of treatment — so far as these can be gauged by the amount of sugar excreted.

(5) The stability of the handy and cleanly carmine test is an unquestionable gain: though this property belongs in an equal degree to the cupric test-paper.

II. The Cupric Test-paper.

The Cupric test-paper.—A large number of observations and experiments have shown me, that the only cupric salt that can be selected as the reagent of a reliable test for glucose in the form of test-paper, is the tartrate of cuprammonium: and it is remarkably well fitted to serve this end, for it is the only compound of copper that is permanent on exposure to the air, and

moreover, the only one that is stable when boiled with an alkaline carbonate—as well as with a caustic alkali; no cuprous oxide falling until a reducing agent—such as glucose—is added. I have now kept test-papers, charged with the cuprammonium tartrate, continuously exposed to light and air for considerably over twelve months, without the slightest change: their glucose-detecting power remaining as definite as when the papers were freshly prepared.

The test-paper is a compound one: consisting of two papers combined by a layer of rubber—one charged with the reagent, and the other with carbonate of soda. Experiment has shown that in order to secure the requisite degree of sensitiveness, the constituents must be in definite proportions.

The reaction.—When the test-paper is dropped into 60m of soft or distilled water, and heat is applied to the boiling point—the boiling being kept up for a few seconds—a greenish tinted solution is obtained, which is perfectly transparent,

and will remain quite clear, though boiled for ever so long. This fact—non-reduction by heat—of course proves the reliability of the test. As the observer lets fall a drop of saccharine urine into the solution, left quite hot on the withdrawal of the flame, he will not note any immediate change: but in a few seconds there will suddenly break out in the body of the clear liquid whitish streaks, that quickly develop into a diffused uniform opacity of a light colour. Renewed boiling deepens the opalescence, which then acquires a yellowish tint. The reaction is, therefore, not a precipitate, like that which falls when Fehling's solution is reduced.

When glucose is present in but small quantity — from 1 to 3 grains in the ounce—the opacity is not only longer in appearing, but is of lighter colour, even after thorough boiling, than when the urine is more saccharine. Observation has shown, that when, after adding one drop of the suspected urine, the solution is kept on the boil, a whitish haze or

opacity will appear towards the close of a minute, if glucose is present in the small proportion of from 1 to 1½ gr. per ounce.

Directions.—1. Drop a test paper into 60m of soft or distilled water.[1] 2. Boil for a few seconds until the water assumes a greenish tint. 3. Extract the papers. 4. Re-boil the solution, and then add one drop of the suspected urine. 5. If glucose be present, reduction will take place without the further application of heat—though, if the observer prefers, he may continue the boiling, and thus hasten the reaction. In any case, if the solution remains transparent for a quarter of a minute, heat should be applied to the boiling point for one minute; if, then, no opacity whatever appears, it may be safely inferred, that glucose in pathological proportions is absent.

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[1] If the water employed be hard, the solution prepared from the test-paper will be milky from precipitated earthy carbonates: if such water be used at all, it should be boiled first of all with a carbonate of soda test-paper, but even then it should not be used for delicate testing. Where the drinking water is hard, rain water should be used.

CHAPTER X.

GLYCOSURIA: QUANTITATIVE GLUCOSE.

The Indigo-carmine Test-Paper provides quantitative information.—A most desirable property of a qualitative test at the bedside is the power to furnish a good notion of the coarser variations of quantity; for, this knowledge obtained on the spot, must often be of greater utility than the discovery of the finer gradations by methods of precision, which are not available beyond the consulting room, and necessarily require time for their application. It is this practical quality which emphasizes the adaptability of the carmine test-paper to bedside work. But inasmuch as almost every saccharine urine provides pretty uniformly the complete reaction — the final pale yellow being nearly always reached—the observer will scarcely be

prepared to regard the test-paper in a quantitative light.

A little observation will, however, soon show, that this aspect of it is not only capable of verification, but can be readily applied in practice.

When the attention has been directed to the degree, and to the rapidity of the reaction with different saccharine urines, great variations are to be observed. In some, for instance, it begins immediately after the drop of urine has fallen into the hot solution, and is perhaps completed in half a minute; while in others, the commencement of it is delayed for twenty or thirty seconds, and pale yellow is not reached until even two minutes have elapsed; and in still others, at the end of the prescribed time for heating—120 seconds—the colour developed is perhaps only red, purple, or violet.

The cause of all this variability is found to be the different proportions of glucose present. This fact I have proved, not only by quantitative estimations by Fehling's solution, but by dissolving glu-

cose in normal urine, and in distilled water, and submitting—as with saccharine urine —one drop of each solution to the test. The reaction — both in the degree it attained in the specified two minutes, and the rapidity of it—was always proportionate to the amount of glucose. For instance, less than five grains to the ounce would not develop the final colour —pale yellow—at all within two minutes, while 10 grains did so within one minute, and 35 or more grains within thirty seconds.

Glucose always afforded the same reaction, whether dissolved in the urine or in distilled water. I therefore conclude, that none of the non-saccharine constituents of the urine are causes of variation. Excessive acidity of the urine may, however, in some cases diminish the reaction; but, inasmuch as from ten to twelve drops of normally acid urine are required to appreciably retard the reaction of a solution of glucose (20 grains to the ounce) on the carmine paper, it is pretty clear, that the acidity

of a urine must rise very considerably over the average, before it can become a source of disturbance. But, inasmuch as saccharine urines are highly acid, and more particularly so after the lapse of a few hours, it will be as well to eliminate this possible cause of variation of the reaction, by adding on all occasions a carbonate of soda paper to a definite portion of the urine to be examined.[1]

On diluting saccharine urines further evidence of the quantitative power of the test-paper is apparent, the reaction being delayed or rendered incomplete—as the case may be—in proportion as water is added to the urine. (See p. 189).

The Mode of Testing.—The directions for the qualitative testing (see p. 164) are to be followed, but with more care in certain particulars.

(1) The water to be used should be distilled or soft.

(2) The quantity of water to be added

[1] There is sufficient soda in each carmine paper to neutralize at least forty minims of urine of average acidity.

should not exceed the 60m mark on the half-inch test tube. A wider tube than this should not be used.

(3) Twenty minims of the urine to be examined are shaken with a carbonate of soda paper in the larger test tube, which is then set aside.

(4) The observer should select, if possible, daylight; and he should place some light coloured object close behind the tube, so that he may view the colour changes distinctly by a bright reflected light. The disappearance of red is, however, perhaps most easily detected by holding the tube against the sky.

(5) Before the testing is begun the observer lays before him his watch—a centre seconds is by far the best for the purpose. Time is to be accurately estimated by the seconds hand.

(6) Immediately after the paper—which is allowed to remain—has been boiled, when the carmine has well passed into solution, and when the liquid is quite hot, one drop—not more—of the urine in the larger test tube is delivered from the

pipette held vertically,[1] and the exact time by the seconds hand of the watch is noted.

(7) The solution is then well boiled up for about 10 seconds, and the tube is raised a few inches above the flame, and is very steadily held in that position; but on the slightest ebullition occurring, it is raised still higher. The prevention of simmering during the course of the heating is a most important precaution towards obtaining reliable comparative results. The slightest shaking of the tube—especially towards the end of the reaction—should be avoided.

(8) If the complete reduction, indicated by pale yellow, is not effected within two minutes, the heating is kept up for the whole of this period.

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[1] I am aware that a drop is a somewhat variable quantity: it is, however, I think preferable—in handiness and practicability—to the minim, the accurate measurement of which requires well trained and reliable eyes and fingers, unfortunately not possessed by all; and the variability of the drop, when discharged from the pipette held in a vertical position, is not so great as to disturb the conclusions of the text. Those who prefer a more precise method will find it convenient to take 10m of the urine, and make up with water to 100m, add a carbonate of soda paper, and use 5m at each testing.

The carbonate of soda paper should on no account be used along with the carmine test-paper, which is complete in itself.

From the time of dropping in the urine the observer should specially note the colour of the solution at the close of

(*a*) Thirty seconds.

(*b*) One minute.

(*c*) Two minutes. (See diagram p. 188).

Quantitative data.—The quantitative information to be derived from the test-paper is obtained from submitting to it the urine, (1) undiluted, and (2) definitely diluted.

1. *The Urine undiluted.*

The data provided fall into two sections: according as the reaction is complete or incomplete at the expiration of the period prescribed for heating—*two minutes.*

(*a*) *The reaction is incomplete.*—When the final colour change—pale yellow—is not developed, there are less than 5 grains of sugar to the ounce, or under 1 *per cent.*

Any vestige of red tinging the yellow

can be distinctly seen, when the tube is held *without any shaking* about an inch before a piece of white paper: on, however, placing it immediately against the latter, a trace of red may still be detected —to remove this requires not less than 10 grains to the ounce.

When sugar is present in smaller quantity than 5 grains to the ounce, the colour of the solution at the end of the heating for two minutes represents definite quantities.

Colour.		*Grains to the ounce.*
Violet[1]	=	about 1.
Purple[1]	=	,, 2.
Red	=	,, 3.
Reddish Yellow	=	,, 4.

If violet does not appear within half-a-minute, there are less than 2 grains of glucose to the ounce.

If the solution, however, retains its blueness for twenty or thirty seconds, and then during the course of the first minute becomes violet and purple, the quantity

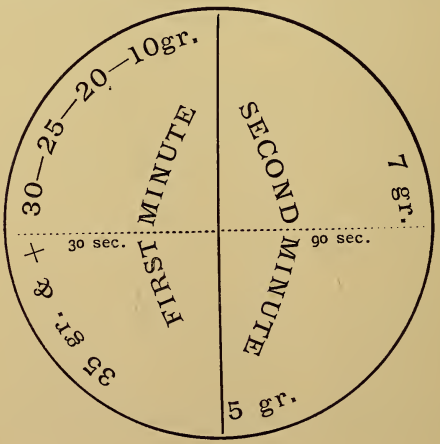
[1] The casual observer is apt to confound violet with purple: but the colours are quite distinct—the former having blue, and the latter red, as the predominating hue.

of sugar is about 2 grains to the ounce: but if the violet appears at the close of the boiling up for ten seconds, there are *at least* from 4 to 6 grains to the ounce.

(*b*) *The reaction is complete.*—The time required for the full development of all the colours is determined by the amount of sugar.

When straw yellow is reached in

	Grains to the ounce.
½ a minute	there are about 35 grains or more.
1 ,, ,, ,, ,,	10 ,,
2 minutes ,, ,; ,,	5 ,,



The observer should carefully note the rapidity of the reaction in the course of the first minute. If at the close of the first half of it the solution is reddish, the quantity will be less than 35 grains to the ounce: but if it is pale yellow, the amount will be larger than this. If at the termination of the minute a red tinge is still apparent, the proportion will be under 10 grains to the ounce, or below 2 *per cent.*

2. *The urine definitely diluted.*

When the reaction with the undiluted urine is completed within one minute, only a general conception of the quantity of sugar is provided by the test-paper. But the information thus obtained is a useful preliminary to the acquirement of a more definite idea of the amount, which can be attained by the further testing of the urine methodically diluted.

The principle of the procedure is to take a measured portion of the saccharine urine (20ɱ) and to dilute by the same volume (20ɱ) of water at a time, until at

last it is found, that at the conclusion of the heating for the definite period of *one minute*, the colour developed is no longer pale yellow, but has a distinctly red tinge; the approximate amount of sugar is then arrived at, by multiplying the number of times the volume of the urine was increased on the previous dilution by 10 grs. to the ounce. In this way, when urines are found to contain more than this amount of sugar, they are uniformly reduced to it; and the dilution is continued until it is clear the limit has been overstepped — a reddish hue remaining at the close of the procedure.

On returning the urine contained in the pipette to the large test tube into which 20m were delivered (see p. 184), the observer adds the same measure of water. If, however, on testing the undiluted urine he found the yellow to appear at the end of half a minute, he may at once dilute the urine to three times its volume (second dilution), otherwise he will only add 20m of water, and re-test. If, at the termination of the

minute the yellow still appears, the contents of the pipette are returned to the test tube holding the diluted urine, and a further addition of 20 $m\mu$ of water is made. The testing is repeated; but, when it is evident the complete reduction of the blue carmine is not accomplished at the expiration of the minute, the procedure is at an end.

On putting this method into practice under the guidance of Fehling's quantitative determination, I find, that when the testing by the carmine paper affords a reddish yellow tint, the value of the last dilution should be counted as five grains; which amount should be added to the 10 grain values of the previous dilutions; but, when the final trial provides a more decided red colour the calculation should only include the previous dilutions. For example: a urine containing according to Fehling 7 *p. c.* of sugar, or about 36 grains to the ounce, on the second dilution, gave at the expiration of the minute a reddish yellow reaction; therefore, the amount was $3 \times 10 + 5 = 35$ grains to the ounce.

Another urine, shown by Fehling to contain 6 *p. c.* of sugar, or about 31 grains to the ounce, just reduced the carmine on the second dilution, but on the third it failed in doing so, and the solution, on being heated for the minute, merely acquired a redness that could not be mistaken for yellow; the calculation was, therefore, $3 \times 10 = 30$ grains to the ounce.

The determination of sugar by this method does not usually require more than three test-papers in all (often two will suffice), and the expenditure of more time than five minutes.

Conclusions.—(1) The indigo-carmine test-paper enables the clinical observer to discriminate between the glucose charges of different saccharine urines in the course of the mere qualitative testing.

(2) It furnishes definite, though only approximative, quantitative data; sufficient, however, for most of the clinical requirements of the practitioner.

(3) The method proposed for its quantitative use exacts but a small expenditure of time—only a few minutes—and merely

that careful attention to a few essential details, and the ordinary skill in observing and manipulating which it is rightly presumed that most medical men possess.

CHAPTER XI.

GLYCOSURIA: THE CLINICAL SIGNIFICANCE OF GLUCOSE.

Glycosuria is not synonymous with diabetes mellitus.—The fact is not sufficiently recognised by practitioners, that the presence of glucose in pathological proportions in the urine does not necessarily imply the existence of saccharine diabetes: any more in fact than does the detection of albumin in the urine signify renal disease.

The glycosuria is intermittent.—As in albuminuria, so in glycosuria, it is of clinical moment to discover if the constituent in morbid proportions is only present while digestion is going on, and

disappears in the hours of fasting. If in any case this relation can be distinctly made out, the disorder is in all probability not truly diabetic. Dr. Lauder Brunton has pointed out, that simple temporary glycosuria very often occurs in perfectly healthy persons.[1] "If you will examine the urine of several healthy persons a couple of hours after breakfast, it is highly probable that you will find distinct evidence of sugar; for breakfast is a meal at which a much larger proportion of bread is eaten than at other meals, and at which, not unfrequently, a good deal of sugar is taken along with tea or coffee."[2]

Glycosuria of this type will become remittent, instead of being merely temporary or confined to the period of digestion, if the meals follow each other before the sur-charge of sugar in the blood is cleared away—then the urine will contain the largest amount of glucose when digestion

[1] Art. *Diabetes* by T. Lauder Brunton, M.D., F.R.S. Reynolds' *System of Medicine.* Vol. v.

[2] Lettsomian Lectures, 1885, on *Disorders of Digestion* by Dr. Lauder Brunton.

is at its height, and the least quantity—always some—before meals.[1]

These forms of digestive glycosuria are not uncommon among the elderly and the gouty; and they have, moreover, been observed when the portal vein is occluded, as in pylephlebitis or in cirrhosis. They are apt to appear also when sugar is taken in excess, or when the digestion of starch is too rapid, and the glucose thus furnished is absorbed too quickly.

Temporary glycosuria has been recorded after an epileptic seizure, or a convulsive fit of hysteria; during or after a paroxysm of ague; after an attack of asthma, or whooping-cough; after inhalation of carbonic oxide, ether, and chloroform; during an attack of sciatica; after injuries of the cerebral lobes, or of the spine from concussion;[2] after operations on the abdominal cavity; during the

[1] The reader will bear in mind, that in diabetes mellitus—as with the albumin of renal albuminuria—the quantity of glucose rises considerably after meals, and diminishes during fasting: when, however, it is still present as a rule, in considerable amount.

[2] Several cases of temporary traumatic glycosuria are on record.

lodgement of a tapeworm in the intestines; and in the course of the recovery from cholera. Probably also neurotic excitement and worry induce it: we then obtain the so-called 'glycosuric storm' from over-strain, resembling temporary albuminuria from the same cause.

The urine of temporary glycosuria differs from that of saccharine diabetes, in being of normal quantity and appearance, and in furnishing a specific gravity not unusually high.

The Glycosuria is persistent.—This is the essential feature of diabetes mellitus.[1] The characters of the urine are: quantity excessive[2]; glucose from 1 to 10 or even 15 *p. c.*, and furnishing a daily discharge which ranges from ½ an ounce to over 2 pounds; specific gravity high—generally from 1030 to 1050; colour pale and bright; odour peculiar—often whey-like; acidity generally high; and, when

[1] The glucose may, however, greatly diminish or even vanish, during intercurrent febrile attacks, on the approach of death, and in prolonged fasting: and it may disappear under dietetic treatment.

[2] When the daily discharge of urine does not exceed 100 ounces the obvious properties of the urine are normal.

it soils the clothes, it leaves a white deposit of sugar. When kept for a few hours in a warm room, diabetic urine becomes turbid from fermentation products — carbonic acid gas, and the spores and filaments of the yeast plant.

In advanced cases of diabetes, the urine is apt to become albuminous from degeneration of the kidneys.

CHAPTER XII.

CHOLURIA: THE DETECTION OF BILE-DERIVATIVES IN THE URINE.

The Biliary Elements which may appear in the Urine.—Two kinds of liver-derived products are met with in urine: one, the bile-pigment; and the other, colourless—the biliary salts.

I. *The Bile-pigment.*

Visual characters of the Urine.—The bile colouring matter always darkens the urine, and communicates to it a yellowish brown or brownish red colour, or even a shade as dark as that of porter. On shaking up the urine, the observer will note, that the froth is yellow: and on dipping a piece of filtering paper or linen into the urine, it acquires a yellow stain:[1] see the patient's shirt.

[1] The observer may thus conveniently take home some of the bile-pigment for examination: for the dried filtering paper will readily deliver up its bile-charge to water.

Very dark bile-charged urines differ from other deep coloured urines, by becoming brownish red or yellow on being diluted.

The Reaction with a Citric test-paper.—The test-paper is placed on the blade of a knife, and two drops of the urine are let fall upon it; heat is applied gradually, and before the paper becomes dry, it turns green or greenish—from biliverdin induced by the action of the acid on the bile pigment—if the dark colour of the urine is due to biliary colouring matter: otherwise the appearance of the paper undergoes no change. A slight reaction is increased by repeating the testing. Care, of course should be taken not to char the paper.

II. *The Bile-salts.*

The Urinary Derivatives of the Biliary Salts.—The salts of the bile-acids, as they exist in the bile, are taurocholate and glycocholate of sodium—the former greatly predominating. These biliary constituents are not altogether eliminated by the kidneys in the chemical

forms in which they are secreted by the liver. When they reach the intestines, they are split up into taurin and glycin on the one hand, and cholate of sodium on the other. The cholate is mainly re-absorbed by the bowels: a small portion only being excreted in the fæces; while the rest is returned to the liver by the portal blood, and is, at least in part, eventually discharged in the urine (see p. 223). The bile-salts, as they appear in the urine, consist of the liver-secreted salts—taurocholate and glycocholate—and of the derived salt—cholate.

The Clinical Tests hitherto employed for detecting Bile-Salts in the Urine are unsatisfactory.—All the works on physiology and on urine refer to Pettenkofer's test—sulphuric acid and cane sugar—or some modification of it, as the only clinical means by which bile-acids are to be detected in the urine. However satisfactory this test may have proved itself in the hands of chemists, who have applied it to solutions of the bile-acids extracted from the urine, it

cannot, I am fully persuaded, claim an analagous position as a mode of direct testing—such as the practitioner requires; for my experience of it as a clinical test has been most disappointing. In delicacy it falls far short of the clinical needs of the practitioner; and in reacting with other substances besides the bile-derivatives—*e.g.*, albumin, and other organic bodies—it is apt to mislead the observer. I can, therefore, endorse Dr. Tyson's remarks on this point.—"From a perusal of almost all the text-books on physiology, and even of numerous manuals on the examination of the urine, the student is led to suppose that the detection of bile-acids, if present in the urine, by means of what is called Pettenkofer's test, is one of the easiest possible. On the other hand, nothing is farther from the truth, and the fact is that *such detection by the direct application of the elements of Pettenkofer's test to urine, or any other animal fluid, is practically impossible, even if the bile-acids are present in considerable amount.* Nor have any of the modifications of Pettenkofer's

test, recently announced as clinically available, proved such in my hands, even where the elements of bile have been added to the urine, except where inspissated ox-bile has been used."—The italics are Dr. Tyson's. (*Op. cit.* p. 91).

I am disposed to conclude from my observations that Pettenkofer's test does not react *directly* with the liver-secreted salts—taurocholate and glycocholate—but only so with the derived salt—cholate. Hence, it does not indicate the presence of the biliary salts in fresh ox-bile until it has had time to decompose them, and thus to liberate cholic acid: but it reacts at once, and very decisively, after the bile has been boiled for several hours with caustic potash—a procedure that breaks up the liver-secreted salts, and furnishes the derivative, cholate. This is doubtless the reason why Pettenkofer's test reacts with inspissated, though it fails to do so with fresh bile—for the taurocholate is readily decomposed by boiling only, and the extract is an evaporation-product; and, furthermore, why it

rarely affords at once a distinctive reaction in jaundiced urines, which are highly charged with liver-secreted salts.[1]

The test for peptones, recently introduced by Dr. Randolph, of Philadelphia, (see p. 90), may likewise be employed for the direct testing of bile-salts: and for this purpose it is delicate; but is unfortunately open to the objection, that it reacts equally well with the merest trace of peptone — a constituent often present in small quantity in the urine of hepatic cases, and moreover, generally in such traces as to be detected with difficulty, and, therefore, cannot always be definitely excluded.

The proposed test is founded on a Physiological Reaction.—The test I employ, for the direct detection of the bile-salts in the urine, is a purely physiological one: for, it is based on a reaction

[1] Just lately I met with an instructive instance, of this fact in a specimen of colourless bile extracted by aspiration from the gall-bladder of a jaundiced patient. I first of all determined the presence of a fairly large quantity of bile-salts. Pettenkofer's test, however, afforded no reaction within several hours; but, after boiling a portion of the colourless fluid with liq. potassæ, the test furnished the characteristic colour change in a few minutes.

which belongs to the bile itself as it flows into the intestines. When the products of gastric digestion—peptone and parapeptone—which leave the stomach in a state of acid solution, meet with the bile, they are precipitated, as a tenacious layer, all over the villi of the lining membrane of the duodenum.

A solution of the Bile-salts precipitates Acidulated Albuminous Urine, or Urine charged with Peptone.—The same physiological fact is illustrated, outside the body, by acidulating—by means of citric or acetic acid—albuminous urine,[1] or urine charged with peptone, and treating it with a solution of the bile-salts—or by ox-bile freed from pigment, mucin, and fat; when the proteid is swept out of solution. This precipitation of albuminous matter from

[1] Physiological writers assert that the bile only precipitates the proteid from the acid solution that enters the duodenum, when in the form of peptone and parapeptone; and not when in that of albumin—as when albumin is dissolved by an acid. If this be so in the duodenum, it certainly is not so in the urine. When a solution of bile-salts is added to an acidified albuminous urine, the proteid is precipitated, just as in the case of acidulated normal urine artificially charged with peptone.

an acid solution is induced, not only by the bile-salts—taurocholate and glycocholate—but also by their derivative—cholate of sodium.[1]

Why not employ an Acidulated Solution of a Proteid in order to detect the presence of Bile-salts, or the derivative of them, in the urine? Hence, as this reaction is a thoroughgoing and decisive one, why not utilize it as a means of discovering the colourless bile-derivatives that may overflow into the urine? For, if these biliary constituents are present, in however small a quantity, they will surely precipitate an acidified solution of a proteid—resembling

[1] There are several conditions that prevent the reaction between the bile-salts and an acidified solution of albumin or peptone: viz., (*a*) an insufficiency or an excess of acid; (*b*) the proteid in large quantity; and (*c*) the bile salts deficient or in great excess. The precipitate with the solution of albumin or peptone, or with urine containing either proteid, dissolves on adding acetic acid, or a citric test-paper to бопт. These facts appear to me to be interesting in connection with the temporary albuminuria or peptonuria which is confined to the digestive periods, and with the increased elimination of albumin in chronic renal disease which takes place after meals. May not a sub-acid or a per-acid chyme, or an excess of the ingested proteid, or a deficient or excessive bile-flow, prevent the biliary salts from precipitating—or rather from completely precipitating as in health—the albuminoid materials whioh flow into the duodenum, aud thus permit the premature absorption of them?

in fact the chyme—when brought into contact with the urine. Experiment and clinical observation have proved such to be the fact.

Acidification is a necessary condition of the reaction.—A solution of the bile-salts mixes with albuminous urine without precipitating the albumin[1]: but on adding a drop or two of acetic acid or a citric test-paper to the mixture, the albumin falls out of solution. Then again, if the observer takes equal parts of an albuminous and of a jaundiced urine, and adds a citric test-paper to 60m of the clear mixed urines, he will observe, in the course of a minute or so, a cloud of precipitated albumin collect in the lower part of the tube. In this case the bile-salts present in the jaundiced urine precipitate the albumin—as in the preceding observation: the citric acid merely performing the same duty as when employed in the

[1] When the bile-salt solution is run upon an albuminous urine, or more especially upon a normal urine charged with peptone, but in neither case acidulated, a delicate zone of precipitated proteid appears; which, however, vanishes on mixing up the solution with the subjacent urine: but the opacity is restored by a citric test-paper, or by a drop of acetic acid.

mercuric or ferrocyanic test for albumin.

About twelve months ago I encountered a fact in urine-testing, which at that time I could not explain, nor could I derive light either from books or from my friends: the same patient, on different days, provided me with various samples of albuminous urine, which were divisible by the action of citric or acetic acid, into two classes—one set precipitating freely with the acid, the precipitate insoluble with heat, and the filtrate albumin-free; and the other set unaffected by the vegetable acid. I carbolized a good example of each kind, and set it aside—believing that the explanation would be forthcoming some day or other. On now re-examining these specimens, I find, the one that precipitates albumin by the organic acid, contains a large quantity of bile-salts; while the other has none—or merely a little more than the trace that belongs to normal urine.[1] The precipitant of the

[1] This patient also on several occasions furnished me with specimens containing peptones in the place of most of the albumin. One of these I also carbolized: on re-testing it, I find the peptones still present, with a trace of albumin; and

albumin was, therefore, in this case also, the bile-salts, which remained inoperative, until the vegetable acid was added.

I have lately met with several urines of normal reaction, containing albumin and bile-salts, in which the proteid was precipitated by merely adding an organic acid.

Acidified Albuminous Urine is a test for Bile-salts in the Urine.—When albuminous urine, acidified by acetic or citric acid, is diluted, and run upon jaundiced urine, it will show the presence of bile-salts: for, along the plane of contact of the urines, a sharply-defined white band or zone of precipitated albumin will instantly appear—a reaction which is indeed very striking and decisive.

The Peptone test Solution.—Having got out the fact, that bile-salts when present in the urine precipitate a proteid from an acid solution, it was an easy matter to discover how to apply it as a practical test. On substituting for the acidified albuminous urine an acidulated

on running over it a diluted solution of acetic acid, there instantly appears a beautiful thick pearly-white zone. Bile-salts are present in large quantity.

antiseptic solution of peptone, I obtained a test solution much better in all respects —being readier and more delicate, and withal a preparation devoid of all objectionable qualities.[1]

The Reaction.—When 20♏ of urine, containing bile-salts in pathological quantity, are run into 60♏ of the test solution, an opalescence appears proportionate to the amount of the bile-derivative. It differs from all other urinary precipitates induced by an acidified reagent, in dissolving up completely on adding a drop or two of acetic acid, or a citric test-paper;[2] and in diminishing, but not disappearing, on boiling.[3]

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[1] The following is the formula for the solution:
Pulverized peptone (Savory and Moore) gr. xxx.
Salicylic acid, gr. iv.
Acid acetic (B.P.) ♏xxx.
Distilled water to ʒ8.
Perfect transparency is obtained after repeated filtration.

[2] When, after dropping in the test-paper, the tube is set aside for a minute or two without shaking, the observer will find the portion below quite transparent, and that above still opaque: and, on shaking up the contents, he will disperse the opalescence throughout.

[3] When the test solution is precipitated by bile-salts, the precipitate has the same peculiarities: dissolving when further acidified, and lessening — certainly not vanishing — when boiled.

The opacity is not affected by such warmth as suffices for the solution of urates, or even by a higher temperature than this implies.

When the test solution is run upon urines containing an excess of bile-salts, an immediate and very distinctive reaction takes place where the fluids meet—namely, a sharply defined white band of precipitated peptone: and, on oscillating the tube, so as to mix up a little of the urine with the test solution, the upper part of the column presents an opacity—the density of which is proportionate to the amount of the bile-derivative present—in marked contrast with the transparency of the urine below. On further agitation, a limit is reached when the opalescence diminishes, and perhaps, finally vanishes: then it is restored, on adding more of the test solution.

Delicacy of the Test: Objections.—The test is undoubtedly a very delicate one: for, I have readily determined by it the presence of 1 part of bile-salts in, at

least, from 18,000 to 20,000 parts of a solution of chloride of sodium.

The question will naturally be asked: is there anything, besides bile-salts, in the urine that will react in like manner with an acidified solution of peptone? So far I have failed to put my finger on any such constituent: and I have tried several—among them kreatin, kreatinin, leucin, tyrosin, hippuric acid, and fatty acids (monatomic and diatomic).[1]

Besides this failure to discover in the urine a non-biliary substance that can precipitate the peptone, all the positive evidence hitherto obtained undoubtedly supports the position, that it is a liver-derived product present in the urine, which reacts with the test. The testimony of the facts is cogent in this direction.

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[1] It is well known that a concentrated solution of chloride of sodium in the presence of an acid will precipitate a proteid. When the chlorides of the urine appear in excess, will they react with the test solution? Experiment shows, that when the peptone solution is run upon a solution of salt of any specific gravity less than 1050, no precipitation whatever appears. Therefore, the urinary chlorides are not a source of error: and more especially, when it is called to mind, that a condition of the testing is the reduction of all urines to the uniform specific gravity of 1008.

(*a*) The biliary salts extracted from the bile produce an identical reaction.

(*b*) The liver is the sole organ that furnishes a secretion which precipitates a proteid from an acid solution. All the secretions, except bile, either do not act on the proteids at all—such as saliva—or they dissolve them—such as the gastric and pancreatic juices. And, furthermore, the biliary salts are the only constituents of the bile that possess the property of throwing a proteid out of solution.

(*c*) The test demonstrates, that the proportion of the bile-salt present in normal urine varies in a well-defined manner with the activity of the digestive organs (see p. 225). This clearly shows that the substance that reacts with the test is intimately connected with the digestive process.

(*d*) Clinical experience. (See Ch. xiii.)

I have checked mucin and urates—the fallacies to which all acid urinary tests are liable.

Mucin.—I have already pointed out

that mucin in acid solution is not precipitated by the addition of further acid (see p. 110). So that when this constituent is thrown down in urine of acid reaction, it seems highly probable that the acid added is not the reagent, but merely supplies the requisite degree of acidity to enable the precipitant already present to operate—as in the case of the bile-salts and albumin (p. 207). If so, a mucin precipitate merely indicates the presence of bile-salts. Furthermore, on running the test solution on the muciparous mixture of normal urine and clear saliva, the reaction is rather diminished than intensified. Then again, the methods of observation, requiring a uniform low specific gravity, obviate a liability to error from this cause (p. 215).

Urates.—Inasmuch as the modes of testing—both qualitative and quantitative—require the uniform dilution of the urines to the specific gravity of 1008, a condition is provided which secures the solution rather than the deposition of urates: so that all observations may be

trusted, without the necessity of resorting to warmth as a corrective.

The mode of preliminary testing.—In every case the urine to be tested must be quite clear. If turbid from urates, it should be clarified by warmth: if from phosphates, very small pieces of citric test-paper should be added and skaken up with the urine, until it becomes transparent—special care being taken not to acidify beyond this limit. It is, upon the whole, best to filter turbid urines: and this proceeding is necessary if the cause of the opacity is organic, or doubtful. When the urine is cloudy from blood, it should first be boiled,[1] and then filtered—for filtering alone does not clarify it.

The specific gravity of the urine is to be reduced to 1008 (p. 48). The object of this direction is to obviate fallacious inferences apt to be drawn from reactions with urines of varying densities—concentrated urines often reacting as if there

[1] Boiling the urine does not destroy the bile-salts. It is true, if any taurocholate of sodium is present, it is broken up: the products being taurin and cholate of sodium. But the peptone test reacts with the cholate as well as with the liver-secreted salt.

were present an excess of bile-salts: and urines of low specific gravity, though sometimes affording a reaction similar to that of normal samples, actually containing an increased proportion.

Twenty minims of urine are added to 60ɱ of the solution.

If the bile-salts are present in excess a distinct milkiness appears, which develops somewhat further in the course of a minute or so: and the depth of the opacity is proportionate to the amount of the bile-derivatives.

If the urine contains the average proportion found in the majority of healthy urines—or, of course, less than that proportion—the reaction is a mere tinge of milkiness, and is, moreover, not immediate.

The 'contact method.' When the test solution is gently run over a urine (reduced to the sp. gr. of 1008) containing bile-salts in pathological amount, an immediate reaction takes place (see p. 211): but when the quantity is normal or sub-normal, the reaction is not instantaneous—it gradually appears in the course of a minute as a

delicate thread-like line, which may undergo a little further development during the lapse of a few minutes.

Quantitative estimation. — Clinical observation demands something more definitely comparable than can be derived from the mere qualitative testing: for, it should decide as accurately as possible the quantitative variations of the urinary elimination of the bile-salts observable in different pathological conditions, in the various stages of disease, and in the effects of treatment. I have, therefore, devised the following procedure to meet this requirement.

The only additional apparatus required is a permanent standard of opacity (see ch. xiv.), to represent the average discharge of bile-salts in healthy urine. The opacity is that provided by mixing together, in equal proportion (60♏), the urine—reduced to the sp. gr. of 1008—and the test solution.

To 60♏ of the test solution, the urine of sp. gr. 1008, is added—in ordinary cases 10♏ or 20♏ at a time, and allowing a minute to elapse after each addition

—until the opacity induced is seen to be exactly equal to, or to slightly over-step, that of the standard—the tubes being held to the light, *shaded by a dark background*, such as that of the coat-sleeve.

If 50m or 60m of the urine bring up the opacity merely to that of the standard, the proportion of bile-salts is not outside the normal range—in the direction of increase. But any smaller quantity of urine required indicates an excess of the biliary derivatives over the physiological variations. The smaller the amount of urine needed, the larger the proportion of bile-salts present—according to the following table :—

Urine. *Minims.*		*Drops.*		*Percentage increase of bile-salts over the normal standard.*
1	or	2	=	6,000
2	,,	4	=	3,000
3	,,	6	=	2,000
4	,,	8	=	1,500
5	,,	10	=	1,200
10	,,	20	=	600
15	,,	30	=	400
20	,,	40	=	300
25	,,	50	=	240
30	,,	60	=	100
35	,,	70	=	83
40	,,	80	=	66
45	,,	90	=	50

Charges of bile-salts beyond 700 *per cent.* increase over the normal average amount, are only met with now and then: but they may be encountered in isolated samples of even non-jaundiced urine; as in a specimen I lately examined containing 1,500 *per cent.* increase of biliary salts, but quite free from bile-pigment.[1]

The Peptone Test-paper.—In accord with the purpose of this little book, I have arranged the peptone test in the form of test-paper, so as to serve the convenience of observers in the preliminary testing. The test-paper is permanent and reliable, and is best used in the following manner:—

The peptone test-paper along with half a citric paper is dropped into 50m or 60m of water in the larger test tube or a wine glass: after the lapse of a minute or so the solution is slightly agitated, and, on being set aside for another minute,[2] is ready for use.

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[1] Pettenkofer's test afforded at once a beautiful reaction with this sample.

[2] The solution thus left at rest for a short time becomes quite transparent,

The solution thus prepared is taken up by the pipette, and carefully run over the transparent urine: when if bile-salts are present in larger amount than the normal average, an immediate reaction is observed, as a pearly-white thread or band; but, with urine devoid of this excess, a delicate zone may appear, but only in the course of from one to two minutes.

The test may likewise be employed equally well in the following ready way:

The test-paper along with half a citric paper is dropped into 60m of water: and 20m of urine, reduced to the sp. gr. of 1008, are added. The contents of the tube are oscillated for half-a-minute, and then set aside for a minute—so as to allow time for the clearing away of gaseous particles and the development of the reaction. If bile-salts are present in excess a distinct milkiness is apparent: but if in normal or sub-normal amount, there is only a slight haze, or no obvious change.

CHAPTER XIII.

CHOLURIA:
THE CLINICAL SIGNIFICANCE OF BILE-DERIVATIVES IN THE URINE.

A mere sketch admissible.—As in the case of albuminuria and glycosuria, so in this, I can but provide in this little work merely an outline of the clinical bearings of the biliary derivatives in the urine, and leave each observer to fill in the sketch with the pencil of his own experience.

The Bile-coloured Urines of Jaundice represent but a portion of the Urines charged with Biliary Derivatives.—According to my observations jaundiced urine is but a section of the large group of urines containing biliary matter in pathological proportions. Hence, I venture to coin the term 'choluria' in order to tersely indicate the

presence of bile-elements—the colourless ones in particular—in abnormal quantity in the urine.

I. The Bile-Pigment.

The presence of the biliary colouring matter in the urine characterizes jaundice from whatever cause.

Apart, however, from jaundice—as ordinarily recognized—bile-pigment in small quantity may temporarily appear in the urine: as in the acute disturbance of the liver that belongs to bilious attacks; but, whenever this is the case, a diminutive form of jaundice may be said to exist, which, were the biliary embarrassment to continue long enough, would declare itself in the ordinary symptoms.

An excess of the colourless bile-derivatives always accompanies biliary pigment in the urine.—So far as my observations have extended, whenever I have met with bile-pigment in the urine, the peptone test has invariably demonstrated the presence of the biliary salts in large quantity (see p. 234). Hence,

provisionally, I am led to regard the term 'jaundiced urine' as synonymous with that of 'pigmentous choluria.'

II. The Bile-Salts.

The Physiological Variations of the Renal Elimination of Bile-Salts.

Bile-Salts in healthy urine indicated by the Peptone Test.—Some few years ago that sagacious observer, the late Dr. Murchison, remarked that "not only in jaundice, but in health, a portion of the bile pigment, as well as of the bile acids, formed in the liver, is absorbed into the blood": if so, may we not expect to find a small quantity of the central components of the bile (the biliary salts), or a derivative of them, in healthy urine? — providing, of course, they are not completely broken up by chemical action,[1] and the mode of direct testing is sufficiently delicate for the purpose of detection. When it is remembered, that

[1] Frerichs as well as Murchison believed that the bile-acids normally absorbed into the blood from the liver were metamorphosed by oxidation into other products.

in man the liver secretes on an average each day not less than 4 ounces[1] of bile-salts, it will surely not be surprising, if a fraction—as it were—of this large quantity should, under the ordinary conditions of health, get adrift from the portal into the general circulation, and be discharged by the kidneys: in fact, were the amount of these leading biliary constituents but half that just indicated, the non-appearance of a small portion of it in the urine would, I think, be regarded by most physiologists as improbable—being contrary to anticipation suggested by kindred data. Certainly so far the biliary salts of the blood have not been isolated: but their absence cannot be inferred from this negative evidence, for the quantity is doubtless too small for separation and detection by the methods hitherto employed. It is not so, however, with the urine: for the bile-acids have been separated by Naunyn and Draggendorf in healthy non-jaundiced urines; and

[1] According to Bidder and Schmidt the daily bile-flow of a man, weighing 140 lbs., is about 50 oz.; and the charge of bile-salts over 9 *per cent.*, or a little over 4 oz.

lately Lépine and Guérin have shown that the greater part of that portion of the unoxydized sulphur present in the urine which is oxydized with difficulty by reagents, is derived from the bile, by the re-absorption of taurocholic acid.[1] Then again, it has been demonstrated that taurin—derived from taurocholic acid—is eliminated in small quantity by the healthy kidney. I, therefore, conclude that the diminutive reaction of the peptone test solution with normal urines accords with the presence of a trace of bile-salts discovered in them by physiological chemists: and from several observations I am disposed to estimate the average amount as about 1 part in from 10,000 to 15,000.

The amount of Bile-Salts present in the normal urine of the same individual varies at different periods throughout the twenty-four hours: the causes of variation.—A large number of observations on the urine of healthy persons with the peptone solution has demonstrated the fact, that the colourless

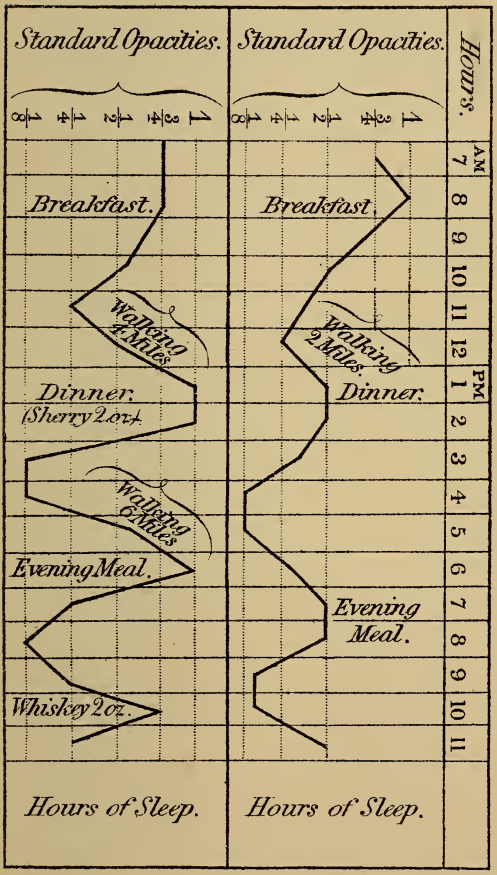
[1] See the *Lancet*, vol. i., 1885, p. 307.

biliary derivatives are discharged by the kidneys in varying proportions at different times in the course of the day. Though always present, they are increased at certain periods and diminished at others: and I find this variation definitely hinges on the digestive act.

The diagrams on the opposite page represent hourly estimations of the bile-salts in the urine of a healthy adult, aged 44, on two consecutive days: when every sample of urine was reduced to the uniform specific gravity of 1008; and the degrees of opacity, induced by mixing 60m of the diluted urine with the same quantity of the test solution, were registered according to a determined scale represented by the figures 1, $\frac{3}{4}$, $\frac{1}{2}$, $\frac{1}{4}$, $\frac{1}{8}$. The reader will observe that the maximum amounts appear during the periods of fasting—as in the urine passed in the morning and before meals; and that the proportion falls quickly—generally in an hour—after each meal, and attains its minimum in from three to four hours.

It would, therefore, appear that the

The hourly elimination of Bile-salts by the Urine: shewing the effects of digestion and exercise.



renal elimination of the biliary salts is the converse of the bile-flow into the duodenum: for, according to the facts provided by biliary fistulæ established in the dog, the discharge of bile into the bowel rises rapidly immediately after eating, reaches its maximum in from two to six hours, and returns to its minimum by the time of the next meal; but never ceases—even though fasting is prolonged.

According to my observations this central fact is modified by various hygienic conditions: among which exercise is the most powerful. On comparing the diagrams — one representing the subject walking only two miles, and the other ten miles—the reader will note, that when the exercise was insufficient, the waves of increased elimination before dinner and the evening meal were imperfectly developed — attaining to merely the half standard opacity; and that, when the walking was extended to ten miles, the renal discharge of the biliary salts following the digestive fall reached the highest degree. It is pretty clear that moderate

exercise invigorates the digestive process: for, with a fair amount of walking between meals, the withdrawal of the bile-salts from, as well as the return of them to the urine, is rendered more decisive and speedy than when a lounging life is led. Indolence, therefore, either favours the retention of these colourless excreta within the systemic blood (cholæmia), or causes them to linger within the limits of the portal circulation, and prolongs each digestive effort.

The systemic overflow of the biliary salts is probably influenced by other hygienic conditions: such as meteorological changes of temperature and of atmospheric pressure; the nature of the diet; and alcohol. Though I have not yet studied with sufficient care the effects of alcohol on the renal elimination of these elements, I think I am justified by the few data observed, in expressing the belief, that in the first instance, it is a checking agent, and then—after inducing congestion of the liver—it brings about an increased discharge, which may be even

detected during the periods of digestion —when ordinarily the renal overflow of the biliary excreta is at its minimum. Should these positions be confirmed by further observation, it would seem as if alcohol should be classed with indolence as a cause of cholæmia and congestion of the portal system: and is, therefore, the opposite of exercise.

The reader should be reminded that the urine of patients does not present such great variations in the amount of bile-salts as are indicated by the diagrams constructed from hourly observations: for, as a rule, it is allowed to collect in the bladder for several hours together, and thus acquires a more uniform charge. When, however, the bladder is cleared just before a meal, the urine voided two or three hours afterwards will in health show the digestive withdrawal of the biliary salts. In order to judge of the renal elimination of these constituents the observer should select the urine of fasting —before breakfast—and of digestion—two hours after breakfast: or he should obtain

a sample of the whole twenty-four hours' discharge.

The clinical significance of the renal excretion of biliary salts.

Data provided by experiments on animals.—A review of the facts furnished by the injection of the bile-salts into the blood of animals (mainly dogs) forms a fitting introduction to the study of the clinical aspects of the renal excretion of these colourless biliary derivatives.

The following symptoms and structural changes have been recorded by several observers (Feltz, Ritter, Röhrig, Albers, and others.)

(*a*) Pulse and respiration retarded.

(*b*) Arterial tension and temperature lowered.

(*c*) Food refused, and loss of flesh rapid. Vomiting of bile and blood.

(*d*) Diarrhæa: bilious, sometimes bloody.

(*e*) Hæmolytic changes, capillaries obstructed and hæmorrhages. The blood more fluid than normal, and less coagulable. The red discs dissolved, and the serum red-coloured from liberated hæmo-

globin,[1] and milky from fat. The passage of the blood obstructed in the capillaries: the red discs flow together *en masse*.

(*f*) Parenchymatous degeneration of glands, muscles, liver, kidneys, &c.

(*g*) Tetanic convulsions, followed by coma and death.

(*h*) Urine albuminous, and red from dissolved hæmoglobin.

The symptoms and tissue changes vary with the amount of bile-salts injected: thus, it is always needful to administer large repeated doses in order to induce convulsions, coma, and death; but a small quantity will produce the analogue of a bilious attack, when there is merely observed—retardation of pulse and respiration, lowering of arterial tension, refusal of food, vomiting, and perhaps diarrhæa.

The balance between production and elimination.—The biliary products discharged into the bowels are mainly utilized in digestive work: and a certain comparatively small portion of them must

[1] When a solution of the bile-salts is added to a drop of blood under the microscope the corpuscles rapidly disappear.

pass out with the fæces—or good health is out of question: unless, perhaps, the renal elimination can in some degree compensate for the intestinal failure. As a rule, however, when either of these channels, by which biliary matter is normally excreted, is obstructed—and above all when both are embarrassed or blocked—the blood becomes surcharged with the poisonous excreta (cholæmia), and then the experiments on animals become living facts in our clinical experience: the form of blood-poisoning being acute or chronic, mild or severe, or individualized by idiosyncrasy of tissue, or by some special concomitant condition, such as fever and the like.

When, therefore, the balance—which subsists in health—between the production of these poisonous products and their elimination is disturbed, disorder or disease is induced: as surely as the smoky atmosphere of a room is the natural consequence of a narrowed or obstructed chimney.

The clinical observation of the bile-

salts in the urine resolves itself into the detection of an excess and of a check to elimination, or of an insufficient discharge.

The Bile-salts are increased.—My clinical experience has demonstrated an excess of biliary salts in the urine in the following morbid conditions :—

1. *Jaundice.*—Authorities are divided on the question of bile-salts in the urine of jaundice: some (such as Frerichs, Städler, Murchison) holding that they are invariably absent — believing that they are decomposed by the blood; others (Kühne) always detecting them — whatever the form and the duration of the jaundice; and others (Geo. Harley) asserting the presence of them in all cases of obstructive jaundice — while, in fact, bile is being secreted by the liver and absorbed into the blood—but failing to discover them when the liver, from disorganization, ceases to secrete bile. All this diversity of opinion must, I think, be referred either to the defectiveness of the processes employed for the separation of the bile-acids from the urine, or to the

want of a clinical test of sufficient accuracy and delicacy. So far my experience agrees with that of Kühne: for I have invariably found an increase — and generally a very decided increase—of the bile-salts in all forms and stages of jaundice; this even in cases of from one to four years' duration. According to my experience of jaundice, the bile-salts are not only apt to appear in the urine in increased quantity before the appearance of bile-pigment, but to persist for some weeks after the urine has become quite free from it.

2. *Functional disorders of the liver: biliousness.*—The bilious may be broadly divided into two classes; namely, those in whom the liver is loaded with biliary products, either from habitual per-secretion, or from an accumulation of them, which is less or more constant, or is only occasional; and those in whom the secretion of bile is always below the average—sub-secretion.

Acute biliousness.—Those who always 'make' bile, as well as those who suffer from biliary engorgement due to defective excretion, &c., are prone to 'hepatic

storms' or periodical overflows of bile either into the bowels or the blood, or into both: as when there occurs a sudden alteration of arterial tension—as a rise from excitement, or a fall from chilling or other meteorological influence—or when a dietetic error is committed. Then, when the bile-derivatives are absorbed in excess into the blood—as they generally are—the symptoms resemble those of acute poisoning by small doses of the bile-salts in animals: namely, feeble pulse, palor, coldness of the extremities, and a feeling of chilliness throughout, from imperfect filling of the arterioles; slow sometimes gasping breathing; nausea and vomiting; and occasionally diarrhæa. In *migraine* these symptoms, which characterize the ordinary forms of acute poisoning by the bile-salts, are overshadowed by the painful disturbances of the fifth and of the optic nerves: neurotic effects which *may* spring from the same central cause; but in these cases the attack is probably preceded or accompanied by an arrest or a diminution of the renal elimination of the biliary salts,

followed by an augmented discharge which affords immediate relief. In an ordinary attack of acute biliousness the bile-salts flush the blood, and are eliminated in increased quantity, and more particularly so towards the close of the disturbance.

Acute bile-acid poisoning may, however, go beyond the stage implied by the ordinary bilious attack: it may even become so intense as to induce convulsions—which, however, as a rule, subside as the suddenly induced excess of the colourless bile-product in the blood is cleared away, either by the kidneys, or by the bowels, or by the skin; such a severe disturbance is apt to follow an excessive indulgence in alcohol, or the taking of some indigestible article of diet, or of too large a meal.

Chronic biliousness is also a cause of an increased systemic diffusion of bile-salts, and the excessive renal elimination of them. Then the disorder is, as a rule, not purely functional: but depends on hepatic congestion induced by alcohol—the initial stage of cirrhosis; by too good living; or by some obstruction to the portal circulation, as

in heart disease; or by the congestive effects of malaria on the liver and spleen. Cases of chronic biliousness are, however, now and then met with which, though providing an excess of bile-salts in the urine, do not exhibit the ordinary signs of hepatic congestion, and are not referrible to the causes just indicated. But chronic biliousness in the majority of cases arises either from sub-secretion of bile, or the retention of biliary elements in the blood (see p. 247-9). When constipation is a prominent feature in a case of biliousness, as it frequently is, the bile-salts will be detected in greater excess than when the bowels are regular or free: and this is not surprising—for constipation means retention of bile about the portal system; favouring, as it does, a retarded flow in the bile-ducts, and absorption of cholate of sodium contained in the contents of the small intestines and in the fæces.[1] In any case

[1] I have, however, every now and then discovered a decided excess of bile-salts in the urine in cases of biliousness with free alvine evacuations—these being quite loose and bright yellow: as if the biliary elements overflowed into the blood as well as into the bowels.

of hepatic disturbance, whenever the edge of the liver is to be felt below the margin of the thorax, and is sensitive to the touch; or when, without obvious enlargement of the liver, the fingers pressed well under the lower right ribs, elicit tenderness, bile-salts in excess will, in all probability, be discovered in the urine. But on the other hand, these constituents are frequently found in excess without there being any tenderness of the liver.

In chronic biliary derangement I have frequentiy found the bile-salts in greater excess in the urine voided during the period of digestion than in that discharged before meals: *e.g.* two hours after breakfast than on rising.

The urine of hepatic embarrassment, producing acute and chronic biliousness, is that of sub-jaundice: a minimal form of jaundice, which, like the major form, is characterized by a surcharge of bile-derivatives in the blood, and the elimination of them by the kidneys; but differs from ordinary jaundice, in furnishing urine which not only contains a smaller

proportion of bile-elements, but always presents an excess of the biliary salts, while it is only occasionally pigmentous.

3. *Diseases of the liver—apart from jaundice.* I have found an excess of bile-salts in the urine of carcinoma; amyloid disease; enlargement of the liver generally; cirrhosis; and in that of tumours probably hepatic.

4.—*Diseases of the spleen.* In several cases of choluria the liver was enlarged as well as the spleen: but in others the enlargement was confined entirely—or almost entirely—to the spleen; but, notwithstanding the absence of definite hepatic disease, the bile-salts appeared in the urine of these cases in large excess, with a little albumin, and they were not accompanied by bile-pigment. This clinical fact appears to me of noteworthy significance in connection with the distribution of the biliary salts in the viscera: in supporting, in fact, the conclusion to which I am led by experimental data—namely, that these elements appear in large quantity in the splenic pulp;

indeed the majority of my observations suggested a larger proportion of them there than in the parenchyma of the liver. But this important matter demands further enquiry. Should, however, the provisional position be afterwards affirmed, it must throw light on the hæmolytic function of the spleen.[1]

5. *Fever.*—A rise of temperature from whatever cause always induces a systemic excess of bile-salts. With a temperature of 104°, and without any suspicion of liver affection, I have known the renal elimination to exceed 400 *per cent.* increase over the normal standard. Even a slight rise—such as that of 1° or 2°—increases the renal discharge of these elements.

6. *Hæmolytic diseases.*—Dissolution of the blood—and especially of red discs—obstruction of the capillaries, and hæmorrhages are prominent facts in the poisoning of animals by injecting bile-salts into their

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[1] For details on this and other points in connection with this subject I must refer the reader to my paper "*A contribution to the clinical study of the liver viewed through the urine.*" The Lancet, vol. I., 1885.

veins. On turning to clinical experience we find the counterpart of these experimental data.

(*a*) *Anæmia.*—In anæmia the balance, which in health is maintained between the generation and the destruction of the blood corpuscles, is disturbed. There is either a failure in the hæmogenesis, or an increase of the hæmolytic process: determining, as the case may be, a hæmogenic or a hæmolytic form of the ailment. Probably the defect is *generally* on the side of construction: but I have met with several instructive examples of the hæmolytic type, in which there was a considerable excess—pretty regularly and persistently maintained—of bile-salts in the urine; then it was that some attention to the portal organs was indicated, and was of greater service than the ferruginous treatment of the blood state—the pernicious work of the liver apparently causing the failure.

As yet I have not had opportunities of studying, in connection with the bile-salts, *pernicious anæmia;* and *progressive anæmia,*

which has a *prima facie* resemblance to the pernicious form.

In *splenic leucocythæmia* I have found a large excess of biliary salts in the urine: in one case as much as 600 *per cent.* increase; in another over 400 *per cent.*

In *malarial anæmia* (in cases even that did not present recognisable enlargement of the liver or spleen, or other organic changes) I have found a marked increase.

In *hæmoglobinuria* the blood corpuscles undergo rapid and wholesale solution: and the liberated hæmoglobin dialyses into the urine (see p. 32). Since I began to use the peptone test I have merely examined the urine of one case of this interesting ailment — interesting specially from the pathological relationship which it suggests between a suddenly induced hepatic or portal disorder, flooding the blood with the central component of the bile, and the rapid hæmolysis: and in this case a large excess was indicated — no less than 1,500 *per cent.* This observation is certainly suggestive: and it will, I think, be a matter of some clinical interest to ex-

amine hæmoglobinuric urines from this standpoint. Before applying the test the observer should always throw down the albumin by heat, *without acidifying the urine either before or after the boiliug*, and then filter.

(b) Scurvy. In the four cases examined there was a large excess.

Capillary hæmorrhage is also a prominent feature of the cholæmia of jaundice, of leucocythæmia, of diseases of the spleen and liver, and of fevers—at the onset especially. It is also met with in the cirrhotic kidney, which appears to afford a check to the renal elimination of the bile-salts (see p. 247).

The urinary elimination of bile-salts is insufficient.—In sketching this clinical aspect of the subject I must divide the cases into two classes: namely, those in which the bile-salts are present in great excess in the blood and the elimination of them by the kidneys is checked or rendered defective; and those in which the production of them is not excessive, but the renal dis-

charge is subnormal. In all there must be a persistent and increasing retention of these excrementitious matters in the blood—perhaps only now and then relieved by the vicarious efforts of the bowels, or skin, or by an occasional spurt — as it were — of the kidneys.

The production is increased but the elimination is diminished.—When the systemic blood is greatly sur-charged with bile-salts—as in fever, jaundice, certain forms of anæmia—the patient is, as a rule, safe from acute poisoning so long as the kidneys discharge them with freedom: it is true he suffers all the while from the textual degenerations induced by the presence of them in excess in the blood; but, while the charge of them is kept down below a certain dose—as it were—by efficient elimination, he runs no risk of imminent danger. But it is probably otherwise when the kidneys fail to bale out the pernicious material: for, then, it accumulates, and effects further destruction of

the cellular elements, and may even reach that percentage proportion which experiment has shown will induce convulsions and coma—a catastrophe which may, however, be averted for a time by a vicarious evacuation from the bowels, or the skin, or perhaps by blood-letting. In high fever—especially at the onset in children—this is by no means an uncommon event: and it may be that many a fever patient has been sacrificed by the injudicious checking of a critical or vicarious evacuation. It is likewise now and then met with in jaundice: when the patient unaccountably becomes apparently uræmic, or at any rate he is seized with convulsions and dies comatose.

It is, therefore, of some practical importance, whenever there is a large proportion of bile-salts in the blood—as for example, in fever and jaundice—to see that the renal eliminaton of these noxious constituents is sufficiently free: and, when a decided falling off takes place, while the fever is high, or the jaundice is unabated, the observer should be ready to assist

evacuation by other channels, and should be on his guard not to check a salutory vicarious discharge.

The production is not excessive but the kidneys fail to keep pace with it.—I have met with several cases, in which the most feasible pathological reading was blood-poisoning from biliary products; yet there were no grounds for believing the digestive organs much at fault. The only definite fact that could be made out from an examination of the secretions, was a distinct falling off in the renal elimination of bile-salts—a fact which appeared to provide a clue in explanation of the obscure symptoms suggestive of a toxæmia: such as a beclouded listless state of body and mind; good-for-nothingness; melancholy; hypochondriasis; and a sallow complexion, probably due rather to the imperfect filling of the arterioles — permitting a fuller view of the adipose tissue—than to biliary pigment. It is true, the patients of this type frequently—if not invariably—present brown-stained patches on the skin: but such pigmentation is probably

derived from a coloured decomposition-product of the biliary salts. Is there a mild form of cholæmia referrible to premature failure of renal excretory work?

After 60 years renal elimination—as a whole—falls very decidedly, even becoming precarious, notwithstanding the lack of any evidence of structural mischief of the kidneys: and I have known the failure to excrete biliary salts become every now then apparently such as to suggest an explanation why the patient passed for a time into a befogged or curiously muddled condition, or why he was even seized with convulsions—these alarming neurotic effects, as a rule, passing away with an increased renal discharge of bile-salts. Such patients are apt to be classed with the epileptics: and, but for the absence of the ordinary indications of Bright's disease, would doubtless be regarded as uræmic.

I have been rather struck with the fact, that the urines of the cases of the cirrhotic form of renal disease I have examined showed a marked diminution in the proportion of biliary salts: this variety

of Bright's disease being, moreover, rather specially liable to retinal and other hæmorrhages, and to uræmia. In a case of waxy kidney free from definite uræmic symptoms and from *post mortem* signs of uræmia, the urinary bile-salts were never below normal—in fact they were as a rule in considerable excess.

If these observations should be confirmed by further enquiry, the question may arise: how far are the symptoms of uræmia referrible to cholæmia—the grave form of cholæmia that culminiates in convulsions and coma.[1]

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[1] It is out of place in this work to discuss the pathology of uræmia. But without doing so, I may say, that all experimentation on animals up to the present has failed to definitely reveal the cause or causes of this condition: it has negatived all the following constituents of the urine—urea, kreatin, kreatinin, leucin, tyrosin, taurin, urates, hippurates. chlorides, sulphates, phosphates, extractives, ammonia salts (including the carbonate), and urinary ferment; and the only evidence of a positive character which it adduces is in favour of the potash salts. The chemico-vital results of chronic Bright's disease are in all probability due to the retention of several chemical agents: for example, urea or its derivate, carbonate of ammonia, may excite the development of the muscular tissue of the circulatory organs (heart and arterioles); and the bile-salts may play an important role in inducing retinal and other hæmorrhages (see p. 245), nausea, vomiting, diarrhæa, convulsions, coma, and death.

CHAPTER XIV.

APPARATUS.

The mode of urinary testing described in the preceding pages requires for the efficient application of it a set of apparatus, which, from its simplicity and compactness, is undoubtedly well adapted to the aim I have kept steadily in view: namely, to provide the most portable and easy methods for quickly determining the practical aspects of the urine in the course of work.

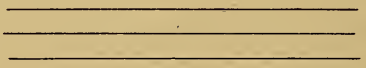
I. Graduated Test Tubes: viz.,

(1). *For determining the specific gravity* (fig. 1) by means of the *glass bead*[1] of the density of 1008 (fig. 5).

[1] The reliability of the method of ascertaining the specific gravity described in Chapter II. depends of course on the correctness of the density of the bead. This all-important point is indeed a matter of no small difficulty with the manufacturer. Every bead sent out *must be carefully tested and if needs be adjusted*, by some thoroughly competent person. The Messrs. Wilson, of Harrogate, have undertaken to do this.

(2) *The tubes for urine-testing—qualitative and quantitative.*

(a) The short half-inch test tube (fig. 2) is used for the qualitative and quantitative observation of albumin, of glucose, of bile salts, and of the reaction of the urine. The lowest graduation measures off 60η. The fractions indicate the amount of albumin expressed as a deposit, when, on adding the albuminous urine, the lines



placed behind the tube are no longer visible (see p. 133).

(b) The flattened tube of determined diametus (not figured), graduated to 200η, is used for the percentage estimation of albumin (see p. 134).

II.—Standard Opacities.

Experience has shown that the best form of permanent opacity is provided by alumina precipitated by ammonia: I, therefore, select it for the standards

required for quantitative observation of albumin and bile-salts.

1. *The standard for quantitative albumin.*—The opaque fluid is sealed up in a short tube having the same diameters as those of the flattened graduated tube in which the estimation is made. The opalescence is that induced by the precipitation of $\frac{1}{10}$ *p. c.* of serum albumin by the mercuric or ferrocyanic test.

2. *The standard for the quantitative observation of bile-salts* represents the average opacity produced by mixing together equal proportions (60m) of the peptone test solution and normal urine reduced to the specific gravity of 1008. It is contained in a short round tube of the same diameter as of that used for testing.

III.—Sundries.

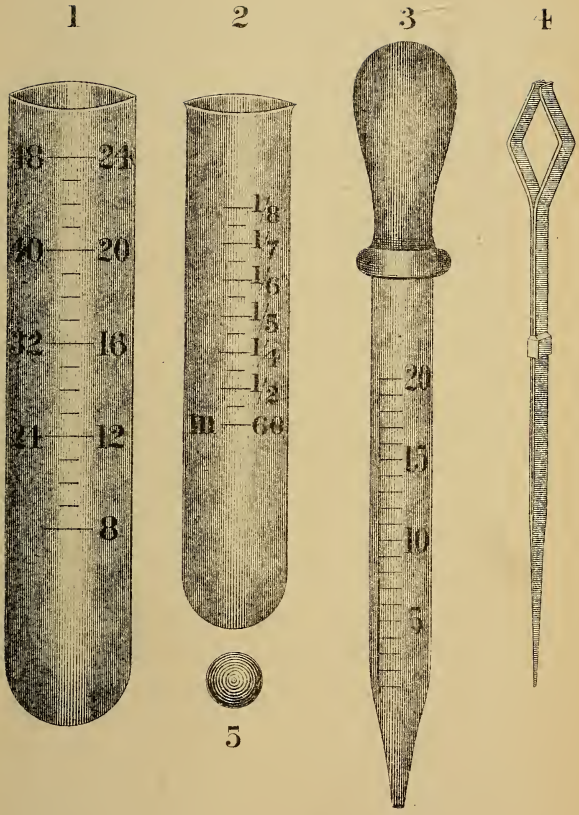
1. *Nipple pipette* (fig. 3).

2. *Metal clip* (fig. 4) used as a tube holder during the boiling and heating required by the testing for sugar, and for drawing out the test-papers, &c.

The whole of the apparatus for bedside observation can be conveniently packed up into a small compass. The pipette—the stem being pushed up within the rubber nipple—along with the clip is inserted into the small test tube, which fits into the stout tube containing the specific gravity bead.

IV. Test-Papers.

Inasmuch as the preparation of the test-papers is all-important, it should be undertaken by some trustworthy person thoroughly conversant with all the necessary details that cannot be conveyed in print. Messrs. Wilson and Son, of Harrogate, have hitherto supplied them to my satisfaction.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ADDENDUM.

I. Mucin and Bile-Salts.

The Reactions of Mucin with organic Acids and Heat.—An alkaline solution of pure mucin (*e.g.*, extracted from bile or saliva) is precipitated by an organic acid: and when an excess of the acid is added, the opacity remains in the cold, but *disappears on boiling*,[1] *and does not return as the solution cools.*

The Reactions of Mucin precipitated by Bile-Salts. — As with mucin thrown down by an organic acid, the precipitate caused by adding bile-salts to an acidified solution of mucin is insoluble in an excess of acid in the cold. Hence, when a citric test-paper is dropped into 60m of a non-albuminous jaundiced urine, a milkiness gradually collects at the bottom of the tube, and rises until the lower half of the column becomes *uniformly* hazy

[1] In the books I see it noted, that the mucin precipitate with organic acids is insoluble with heat: this is so on using only a small quantity of acid; but on the addition of an exeess, solution is easily effected by boiling.

or turbid. I have already pointed out that the albuminous and peptonous combinations with bile-salts thrown down by a certain degree of acidity dissolve on adding the acid in excess (see p. 210). This fact is well shown by dropping a citric test-paper into 60m of albuminous jaundiced urine; when—the tube having been set aside—in the course of a few minutes a *zonular* precipitate develops above the lowest portion of the column, where the urine, from the excess of acid which there collects, remains clear, or is merely slightly hazy from mucin.[1] In this way a citric test-paper affords a good practical distinction between mucin and albumin when bile-salts are present in excess. The opacity which instantly appears on adding a few drops of a solution of bile-salts—care being taken to avoid an excess—to a transparent acidified solution of mucin, and sodium chloride—representing the salinity of urine—vanishes or diminishes with heat: but

[1] If the observer charge a non-albuminous jaundiced urine with some albuminous urine he will readily verify this fact.

reappears intensified on cooling. The like reaction is witnessed in albumin-free jaundiced urines, which always contain much mucin. In experimental testing the effect of heat on the opacity appears to vary with the proportions of mucin, bile-salts, and acidity.

Mucin along with Bile-Salts may mislead the observer testing for Albumin by Heat and Acidification. —When the upper part of a column of jaundiced urine of normal acid reaction remains clear on boiling, the absence of albumin may be pretty safely inferred. But on withdrawing the flame, the observer will produce a very pronounced opacity in the heated part by dropping in a little acetic acid—a reaction not due to albumin brought out by the acidification, but to the precipitation of mucin by the bile-salts present in the urine. It is, therefore, not safe to infer that every opacity which remains after boiling followed by acidification is albumin. This observation must qualify the remarks as to albumin in normal urine contained in the note on

p. 99. My observations on the reaction between bile-salts and mucin lead me to question the reliability of heat with acidification as a test for small quantities of albumin in urine.

II. The Peptone Test for Bile-Salts.

The Urine submitted to examination must not be alkaline.—If the urine is alkaline it should be brought up to a normal degree of acidity by fragments of citric test-paper.

The mode of preliminary routine testing.—In giving the directions for the application of the peptone test I omitted to remark, that in the ordinary course of practice the test solution may be run gently over the native urine: when, if no reaction or only a trace of one appears, the observer may infer that bile-salts are not in excess; but if the zonular precipitation of the peptone is at once apparent, an increase is indicated, and then the specific gravity of the urine should be taken by the bead, and the relative increase of the bile-salts determined (see p. 217).